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## STUDIES IN TUBERCULOSIS.

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### IV: BACTERIOLOGICAL DIAGNOSIS FROM THE GASTRIC CONTENT.[1]

IT must be confessed that clinicians and laboratory workers in Australia have been slow to appreciate the importance of bacteriological examination of the resting content of the stomach as an adjuvant in the diagnosis, prognosis and regulation of treatment of pulmonary tuberculosis. With the application of thoracic radiography to large sections of the population in a manner such as is being witnessed in Australia in the radiological survey of the Australian Imperial Force, and the discovery thereby of many cases of presumed pulmonary tuberculosis among apparently healthy persons, there is the concomitant necessity for effective bacteriological control of radiological diagnosis. It should not be necessary to formulate the grounds on which bacteriological confirmation of radiological diagnosis is essential, nor should the bacteriologist be at the end of his resources if the patient is unable to produce a specimen of sputum.

#### Principle.

Children almost invariably swallow rather than expectorate sputum, and it was with the object of overcoming the difficulty inherent in this fact that Meunier, forty-three years ago, suggested and successfully accomplished the demonstration of tubercle bacilli in the product of gastric lavage carried out on tuberculous children. Meunier's work did not attract the attention which it undoubtedly merited, until it was applied by Armand Delille and Vibert in 1927.[(1)] Since that year many workers in the field of pædiatrics, notably Poulsen, Jensen and Husted in Denmark,[(2)] Wallgren in Sweden,[(3)] and Collis and Brockington in England,[(4)] have established the method as one of great clinical value. The many articles dispersed through American journals devoted to diseases of childhood serve to emphasize further the inexplicable tardiness in Australia in adopting bacteriological examination of the gastric content as a routine measure in the diagnosis of pulmonary tuberculosis

In the practice of aspiration of the gastric content with a view to the disclosure of *Mycobacterium tuberculosis* therein, it is assumed that tubercle bacilli are conveyed to the stomach from an unhealed pulmonary lesion in bronchial mucus which is brought to the pharynx and swallowed. Bronchial secretion may reach the pharynx as the result of coughing or by the action of the cilia of the tracheo-bronchial epithelium; in larger amounts mucus or mucopus of bronchial origin is generally expectorated by adults, but it is not infrequently swallowed. In small quantities imperceptibly secreted it may be transferred from the respiratory to the alimentary system by the process known colloquially as "clearing the throat".

In the vast majority of instances the presence of tubercle bacilli in the gastric mucus may be correctly assigned to a parenchymal pulmonary lesion. In children the contents of a caseating mediastinal lymphatic gland may be discharged into the tracheo-bronchial system, or as occurred in a patient at the Children's Hospital, Melbourne, a few months ago, directly into the œsophagus. Within the last three years I have cultivated *Mycobacterium tuberculosis* from the exudate of tuberculous *otitis media* and mastoiditis in both children and adults; such lesions may discharge tubercle bacilli into the pharynx, as may also

[1] A report to the National Health and Medical Research Council of Australia.

tuberculous processes in the tonsils. Tuberculosis of the gastric mucosa itself is so rare that it may be said not to operate as a confusing factor in the diagnosis of pulmonary tuberculosis by causing tubercle bacilli to appear in the gastric content. Should *Mycobacterium tuberculosis* of the bovine type be recovered from the gastric mucus, consideration must be given to the possibility of the microorganism having gained access to the stomach by the ingestion of raw milk on the part of the patient.

Influenced by the fact that many specimens submitted as sputum do not represent mucus of bronchial origin, but rather a mixture of naso-pharyngeal mucus and saliva in varying proportions, a number of Continental workers, led by Armand Delille, Lestocquoy and Vibert, have applied Meunier's principle to the examination of adults. Scandinavian investigators have sustained a leading part in these researches, as may be gathered from the now extensive literature upon the subject. Two contributions by R. H. Stiehm[2,3] demonstrate the fallacies in findings based upon the examination of sputum of doubtful nature and should convince the most conservative of the necessity for bacteriological exploration of the gastric mucus of patients under clinical or radiological suspicion of pulmonary tuberculosis.

The fertile field for bacteriological activity represented by search of the gastric content of adults for tubercle bacilli is one to which English workers have made a late entry, and Australian workers a still later one. The work of Kane and Hounslow[1] is the only study of this nature to have emanated from England, and the application of the technique under discussion to the bacteriological examination of recruits enlisting in the Australian Imperial Force is to the best of my knowledge the only piece of research of its kind recorded for Australia.

### Technique.

The method has become widely known as that of "gastric lavage" in the diagnosis of pulmonary tuberculosis; but as it has been practised in the pursuit of the results which it is the purpose of this paper to record, the process has been one of aspiration of the resting content of the stomach rather than gastric lavage. Many workers introduce 200 cubic centimetres of distilled water into the patient's stomach and withdraw it after an interval of five to ten minutes. The deposit secured from the washing by centrifugation or prolonged sedimentation is examined for acid-fast bacilli in Ziehl-Neelsen preparations and utilized for guinea-pig inoculation, direct cultivation, or the combination of these methods of detecting *Mycobacterium tuberculosis*. Experience in the examination of gastric content for the presence of tubercle bacilli has led me to abandon any attempt at washing the mucosa of the stomach in favour of simple aspiration of the resting content. Dispersion of a probably small number of tubercle bacilli through a large volume of diluent imposes an unnecessary handicap against their ultimate recovery, for a certain loss of these microorganisms is inseparable from commonly employed methods of concentration. I therefore prefer to avoid dilution of the gastric content and rely upon direct aspiration as effected by means of the Rehfuss tube and a "Record" syringe with a capacity of 10 or 20 cubic centimetres. The volume of the resting content may vary, of course, from 10 cubic centimetres or less to 60 cubic centimetres. Clogging of the apertures in the bulb of the Rehfuss tube by viscid mucus or mucopus is a common occurrence, and the injection of 15 or 20 cubic centimetres of distilled water may be necessary to overcome this contingency. The water so introduced should be allowed to remain in the stomach for approximately ten minutes, during which interval it effects a degree of softening of the viscid material sufficient to facilitate its withdrawal. A few sips of distilled water may be allowed the patient to assist him in the swallowing of the Rehfuss tube; a quantity not more than 20 cubic centimetres may also be introduced into the stomach if the yield by direct aspiration is very small, but for the reason already indicated I avoid the use of larger amounts of distilled water.

It is obvious that the presence of food is highly undesirable in stomach contents secured for bacteriological examination; but another important reason for the selection of the early morning as the optimum time for the collection of the specimen is that reduction of gastric peristalsis to a minimum during the night permits the retention of bronchial mucus should it reach the stomach. In the withdrawal of the gastric content particular care should be taken to secure a sufficient amount of viscid mucoid material.

When young children are being dealt with, the practice at the Children's Hospital, Melbourne, is to pass a rubber catheter into the stomach via the mouth or nose, according to the predilection of the operator. Older children often succeed in swallowing the Rehfuss tube. Adult patients are asked to attend at 9 a.m. and to refrain from taking food or drink after 10 p.m. of the evening preceding the appointment. The procedure after the resting content has been withdrawn and safely deposited in a large test tube or conical measuring glass is determined by the character of the product. In some specimens thick mucus or mucopus is present in surprising amounts and rises to the surface in a manner which enables the required quantity to be "fished" out immediately. In other samples of gastric content lumps of mucopurulent matter settle to the bottom of the test tube within two or three hours; but in many no such pathological constituent is recognizable. When such specimens are being dealt with, the best plan is to place them in the refrigerator and await the result of sedimentation until the following day.

A convenient quantity, for example, six or seven cubic centimetres, of selected material or sedimented deposit is placed in a screw-capped bottle, and no bottle could be better adapted to the purpose than the McCartney bottle, designed as a substitute for test tubes in the cultivation of *Mycobacterium tuberculosis*, and described in the well-known laboratory hand-book of Mackie and McCartney.[4] From this point the measures to be taken are identical with those prescribed in the preparation of sputum for guinea-pig inoculation or direct cultivation of *Mycobacterium tuberculosis*. The examination is undoubtedly made more searching by the employment of both animal inoculation and cultural methods; but as a means of handling the large numbers of specimens derived from Children's Hospital, Army and Air Force sources during the past two years, guinea-pig inoculation presented itself to me as slow, cumbersome, expensive and totally impracticable. I have therefore relied upon direct cultivation and reduced guinea-pigs to the role of supporters of virulence tests.

It is the practice at the Children's Hospital laboratory to examine a preliminary Ziehl-Neelsen film preparation of the inoculum as prepared for cultivation. At this stage tubercle bacilli, if present, are presumably concentrated in the deposits from the centrifuge tubes, and acid-fast bacilli have been demonstrated by direct microscopic search on 15 occasions; four of the patients were children and 11 were adults, all Australian Imperial Force recruits rejected or deferred by reason of radiological evidence of pulmonary tuberculosis. The likelihood that acid-fast bacilli other than tubercle bacilli may gain access to the stomach in ingested food has induced a certain reluctance to accept acid-fast microorganisms found in smear preparations of gastric mucus as tubercle bacilli with the same degree of confidence as attends such findings in the examination of smears of sputum. In every instance in which acid-fast bacilli were found by direct microscopic search of smears of the deposit obtained from the gastric mucus of children, clinical evidence of tuberculosis was so strong that to question the fact that the microorganisms were tubercle bacilli seemed to be standing on an academic point. In these four instances among children the cultural characters of the microorganisms were held to supply sufficient confirmation and virulence tests were not instituted. It was otherwise, however, with certain children, in whose gastric content no acid-fast bacilli could be demonstrated in film preparations, and in whose cases the clinical diagnosis was more or less doubtful. In all such instances the acid-fast bacillus cultivated from the gastric mucus was required to prove its capacity to induce fatal tuberculosis in a guinea-pig.

In the investigation of the adults who contribute the major share of the results shortly to be presented, all of whom were soldiers, a more rigid insistence on virulence tests was maintained. It is to be remembered that all of these men were apparently well and were following their normal avocations at the time of their enlistment. The radiological findings regarding them varied from positive statements of active pulmonary disease, of varying degrees of chronicity, inactivity and apparent healing, to a frankly negative report in one instance. In the case of all these men, irrespective of the character of the radiological reports and notwithstanding the discovery of acid-fast bacilli by direct microscopic search of films of the gastric mucus, cultures of presumed *Mycobacterium tuberculosis* were verified as such by guinea-pig inoculation.

### Results Attending Cultivation of Mycobacterium Tuberculosis from the Gastric Mucus of Children.

It is probably the experience of most pathologists that, given a few positive findings with any newly introduced procedure for laboratory diagnosis, clinicians demand its application with more enthusiasm than discretion. This tendency is evident in the fact that of the 81 children whose gastric content I have been asked to examine by cultural methods for the presence of *Mycobacterium tuberculosis*, 34 exhibited no reaction to the Mantoux intracutaneous tuberculin test. In an account of four years' experience in the examination of the gastric content of children for the presence of tubercle bacilli, Poulsen and Andersen[10] record the recovery of *Mycobacterium tuberculosis* from 199 of 622 children reacting to tuberculin; the same methods applied to 158 children who failed to react to tuberculin yielded not a single positive bacteriological finding. It is legitimate, therefore, to eliminate these 34 children in endeavouring to assess the utility of bacteriological diagnosis from the gastric content, as it is also fair for a busy hospital pathologist to make a positive reaction to tuberculin a condition precedent to the undertaking of such a time-consuming procedure as the effort to cultivate tubercle bacilli from the gastric content.

In addition to the absence of reaction to the tuberculin test, the impressions gained from a study of the case records of the 34 children in question are not such as would suggest their inclusion in a series of tuberculous children. Bronchitis, bronchiectasis, slow resolution of pneumonia, empyema, malnutrition and even scorbutus figure among the diagnoses eventually assigned to these children. Analysis of the case records also indicates five other children from whose gastric mucus the prospect of recovering tubercle bacilli was remote. There remain, therefore, 42 children for whom the clinical presumption of tuberculosis was supported by radiological evidence in the majority of instances, and a "positive" reaction to the tuberculin test in all. *Mycobacterium tuberculosis* was cultivated from the gastric content of 17 (40·5%) of the 42 children in the group, and in four instances promise of successful cultivation was given by the observation of acid-fast bacilli in direct smear preparations of the gastric mucus.

Of the 17 children in whose cases bacteriological diagnosis was established by the examination of the gastric mucus, eight subsequently died. The thoracic radiographs of all except one had been suggestive during life, and in death all the patients displayed tuberculous lesions of the lung parenchyma and tuberculous tracheo-bronchial adenitis, varying degrees of visceral miliary sowing and tuberculous meningitis. In one child erosion of the œsophagus by a caseating and discharging mediastinal gland had established conditions for an almost direct entry of tubercle bacilli to the stomach.

In six other children of the group in which *Mycobacterium tuberculosis* was cultivated from the gastric mucus the thoracic radiographs were interpreted as indicative of pulmonary tuberculosis. Two developed tuberculous lymphadenitis in accessible glands, which provided morbid material from which cultures of *Mycobacterium tuberculosis* confirmatory of those secured from the gastric mucus were obtained.

*Mycobacterium tuberculosis* was recovered in culture from the resting content of the stomach of two children in whom the disease process immediately responsible for their presence in hospital was a pleural effusion; in one instance the existing lesions of *erythema nodosum* constituted a further indication for an attempt to place the diagnosis on a bacteriological basis.

The last child in the group of 17 in which bacteriological confirmation was supplied by the utilization of the gastric content was a little boy, aged six years. The immediate cause of his admission to hospital was arthritis of doubtful ætiology affecting the hip joint. An unequivocal reaction to the intradermal injection of 0·001 cubic centimetre of old tuberculin strengthened the suspicion of tuberculosis based on the statement in the family history that an uncle and an aunt of the boy were subjects of pulmonary tuberculosis. The report on the thoracic radiograph, while noting the presence of calcified hilar glands and enlargement of the hilar shadow on the left side, stated that there was no radiological evidence of a lesion in the parenchyma of the lung. The carious condition of several of the child's teeth and a generally unhealthy state of the gums suggested oral sepsis as an ætiological basis for the arthritis at least as likely as tuberculosis. Diagnosis was therefore an open question, eventually resolved by the recovery from the gastric mucus of an acid-fast bacillus, consistent with *Mycobacterium tuberculosis* in cultural characters and productive of severe and fatal tuberculous lesions in a guinea-pig inoculated by intraperitoneal injection.

Eleven of the 17 children from whom tubercle bacilli were recovered by the method under discussion were less than three years of age, while only one was older than seven years. He was a boy, aged twelve years, who exhibited pleural effusion and *erythema nodosum*; his aunt had died of pulmonary tuberculosis and a brother suffered from tuberculous disease of the hip joint. That the positive bacteriological results were derived in the main from infants and very young children is not surprising, for the younger the child, the less the probability of the lesion of primary infection having healed, and the more frequent the occurrence of progressive disease. The concentration of positive bacteriological findings in the period of infancy and the succeeding two years is well illustrated in the extensive investigation by which Poulsen and Andersen[10] demonstrated the presence of tubercle bacilli in the gastric mucus of 199 children. The series included 62 babies in the first year of life; in no less than 54 instances tubercle bacilli were revealed in the deposits obtained from gastric washings. In the second year of life bacilli were demonstrated in approximately one-half of the patients examined; in the third year, about one-third; in the fourth year, one-fifth.

Table I correlates the leading clinical features and the bacteriological findings in the cases of 42 children who reacted to the Mantoux test.

### *Pleural Effusion.*

The results attending attempted cultivation of *Mycobacterium tuberculosis* from the gastric mucus as a means of establishing the tuberculous nature of pleurisy with effusion have been disappointing. It is difficult to believe that an active underlying tuberculous pulmonary lesion, from which bacilli might have reached the stomach in swallowed bronchial mucus, was present in only two of the 17 children studied on account of the presence of pleural effusion, and the more so as house contact with phthisical relatives was elicited for six of the patients in this group. I feel that the results obtained in this phase of the work are susceptible of considerable improvement. In the general stress of coping with large numbers of specimens of sputum and gastric content from the Children's Hospital, Army and Air Force sources, it has not been possible for Mr. H. Weir and myself, working in a routine hospital laboratory with its many other activities, to carry out the desirable number of "repeat" examinations. The importance of returning to the attack after being defeated in the first attempt is shown in the work of Poulsen and Andersen,[10] to which I have already

TABLE I.

| Clinical Condition. | Examination of Gastric Mucus for Tubercle Bacilli. | | | Remarks. |
|---|---|---|---|---|
| | Number. | Positive Result. | Negative Result. | |
| Tuberculosis of lung parenchyma or hilar glands. | 17 | 14 | 3 | Of the three children for whom a negative result was returned, one was certainly tuberculous, as proved by autopsy. The presumption in the second case was very strong. The child was aged 12 years and had suffered repeated hæmoptyses, and her brother was known to be tuberculous. There was also radiological evidence of pulmonary tuberculosis. Three attempts to demonstrate tubercle bacilli in the gastric content failed. In the case of the third child the X-ray findings were dubious; aged 4½ years, she reacted to tuberculin, and her mother was undergoing sanatorium treatment. |
| Pleural effusion .. .. .. .. | 17 | 2 | 15 | Generally older children; two under two years, one of four years and one of seven; the ages of the remaining 13 lay between 9 and 13 years. The family histories of six disclosed contact with phthisical relatives. One of two from whose gastric mucus tubercle bacilli were cultivated exhibited *erythema nodosum*. |
| Osseous tuberculosis .. .. .. | 6 | 1 | 5 | *Mycobacterium tuberculosis* was cultivated from the urine of two and from the wrist-joint of another of the five children, of whose gastric content attempted culture yielded a negative result. |
| *Erythema nodosum* .. .. .. | 2 | 1[1] | 1 | |
| Totals .. .. .. .. | 42 | 17 | 25 | |

[1] The positive finding has already been included under "pleural effusion".

referred. These workers demonstrated tubercle bacilli in the gastric content of 199 among 622 children examined in this manner. The positive finding was registered for 152 (or 77%) of the patients at the first examination; a second examination raised the percentage to 91, and a third to 96. It would seem reasonable, therefore, to postulate that three bacteriological examinations of the gastric content should be made before a negative finding is recorded. A method that has been adopted with advantage by R. H. Stiehm[6] and others is to aspirate the resting content of the stomach on three successive mornings and mix the selected materal or centrifuged deposits from each specimen; the examination is thereby made more thorough, and economy of time, culture medium, animals and incubator space is effected. Proceeding in this manner, Stiehm succeeded in demonstrating by guinea-pig inoculation the presence of tubercle bacilli in the gastric content of every one of four students affected by pleurisy with effusion.[6]

### *Erythema Nodosum.*

Three children manifested the suggestive combination of *erythema nodosum* and "positive" reaction to tuberculin, and from one, a boy, aged twelve years, in whose illness pleural effusion was also a feature, *Mycobacterium tuberculosis* was cultivated from the gastric mucus.

Ever since Wallgren[9] noted that a preponderating majority of children manifesting *erythema nodosum* reacted to tuberculin at the time of onset of the nodular fever, and proved the presence of tubercle bacilli in the gastric content of 17 out of 37 such patients, a great deal of attention has been centred upon *erythema nodosum* as an expression of tuberculosis. In a later study Phillipson and Wallgren[10] found tubercle bacilli in the material obtained by gastric lavage from 47 of 96 children in whose illness *erythema nodosum* was a conspicuous clinical feature.

Many hundreds of observations are now on record concerning the intimate relation between *erythema nodosum* and tuberculous infection, and a particularly interesting communication of this nature, recording the eruption of *erythema nodosum* concurrently with the development of acute tuberculous cervical lymphadenitis, is that of B. C. Thompson.[11] The conception of *erythema nodosum* as a non-specific inflammatory reaction in the skin, excited by a variety of agents, notably the tubercle bacillus and the streptococcus, is not incompatible with the acceptance of Wallgren's doctrine that *erythema nodosum* should be regarded as tuberculous until it is proved otherwise. Those who would insist on the non-specific nature of the exciting agent in *erythema nodosum* may find support for their contention in the report by Juliet E. Thorner[12] of seven instances of *erythema nodosum* in childhood in which the associated and apparently underlying pathological process was respiratory infection with the fungus *Oidium coccidioides*.

### Results Attending Cultivation of Mycobacterium Tuberculosis from the Gastric Mucus of Adults.

The results now to be presented, obtained from the application of cultural methods to the gastric content of adults, have all been gathered in the course of bacteriological examinations instituted to supplement the routine radiographic investigation of the Australian Imperial Force and the Royal Australian Air Force. A preliminary report on this work as furnished to the National Health and Medical Research Council and the Director-General of Medical Services appeared in *The British Medical Journal* of May 10, 1941. The final report is yet to be written. It is permissible, however, as promoting a discussion concerned specifically with the stomach as a reservoir of tubercle bacilli to be exploited in the diagnosis of pulmonary tuberculosis, to amplify the findings already reported and give them more detailed consideration.

In the course of laboratory work, which has provided bacteriological confirmation of radiological diagnosis of pulmonary tuberculosis in the case of 151 volunteers for enlistment in the Army and of 10 patients of Number 2 Royal Australian Air Force Hospital, acid-fast bacilli have been cultivated from the gastric mucus of 50 men. In 11 instances acid-fast bacilli, subsequently shown by cultivation and guinea-pig inoculation to be virulent tubercle bacilli, were detected by the microscopic search of direct smear preparations of deposit from the gastric content. If six cultures are discounted on the ground that their pathogenicity for the guinea-pig was not satisfactorily established, the number of cultures which may properly be presented as of *Mycobacterium tuberculosis* becomes 44. In order to arrive at the number of men, bacteriological diagnosis of whose condition could not have been provided without recourse to the gastric content, the figure of 44 is to be reduced by seven, as in seven

instances *Mycobacterium tuberculosis* was identified in both sputum and gastric content. One soldier, who could not expectorate sputum at the time he was referred for examination, and therefore submitted himself to aspiration of the resting content of the stomach, reappeared one week later with a specimen of sputum in which numerous tubercle bacilli were evident to direct microscopic examination. The samples of sputum submitted by the other six men were considered of doubtful quality, and the gastric content was withdrawn in order to provide a second string to the bacteriological bow. There were thus 37 men examination of whose gastric content furnished a bacteriological diagnosis which would not otherwise have been forthcoming.

Of the 44 men from whose gastric content *Mycobacterium tuberculosis* was cultivated, the radiological reports with regard to 32 suggested exudative lesions and extensive infiltrations with or without cavitation, and indicated the summary rejection of the recruits on radiological evidence. More interesting from the bacteriological viewpoint are the remaining 12 men, in the case of 11 of whom the radiological findings were of a less positive character, the reports being framed to suggest old, inactive or doubtful tuberculosis, and perhaps including a recommendation for bacteriological examination. The twelfth man was passed by the radiologists and by some accident found his way to the laboratory with others who were listed for bacteriological examination. It may be of interest to record brief details concerning the 12 men, bacteriological examination of whose gastric content was particularly illuminating.

TABLE II.

*Notes relating to a Group of Twelve Men.* Mycobacterium tuberculosis *Cultivated from the Gastric Content: X-ray Findings Suggestive of Old, Inactive or Doubtful Tuberculosis.*

| Number of Subject. | Radiological Report. | Remarks. |
|---|---|---|
| 37 | Scattered calcification; right apex. | Clumps of acid-fast bacilli in direct smear of gastric mucus. Pain in chest 15 months earlier, but was not obliged to go to bed. |
| 137 | Suspicious area in right infraclavicular region, radiating from hilum. Defer. | Product of gastric aspiration thick and mucopurulent. Mother a subject of "bronchitis". |
| 152 | Possible tuberculosis of right upper lobe. | Had never had occasion to consult a doctor; family history clear. |
| 163 | Partially calcified and fibrotic tubercular areas. | Personal and family history clear. |
| 255 | No sign of tuberculosis; pass. | Personal and family history clear. |
| 302 | All tuberculous lesions of right upper lobe quiescent. For bacteriological examination. | No reason to think not quite well; had been told he had pulmonary fibrosis. Family history clear. |
| 312 | Lateral view confirms presence of cavity in upper portion of lower lobe of left lung. Appearances consistent with abscess formation of non-specific character. | Tubercle bacilli found in smear of sputum after growth had been initiated in culture from gastric content. "Always fit"; once coughed blood after an accident. |
| 427 | Old fibro-calcareous tuberculosis of right upper lobe. Reject. | No suggestive facts in personal history. Cousin died of tuberculosis; casual contact only. |
| 487 | Scarring at left apex; bacteriological examination. | Personal and family history clear. |
| 510 | Doubtful nodules in apex of left upper lobe. Bacteriological examination. | Considered himself quite well; pneumonia five years earlier. Frequent colds. |
| A23 | Infiltration in left upper lobe; probably tuberculous. For bacteriological examination. | No symptoms; family history clear; routine X-ray examination. |
| A29 | Old infiltration, apical and sub-clavicular, both lungs; more pronounced on left side. For bacteriological examination. | No symptoms; family history clear; routine X-ray examination. |

*Non-Virulent Acid-Fast Bacilli.*

It has already been indicated that six cultures of acid-fast bacilli derived from the gastric content of recruits providing radiological evidence of pulmonary tuberculosis were discarded as being insufficiently substantiated in the essential attribute of virulence to the guinea-pig. In three such instances the proposed virulence tests were vitiated by the late appearance of contaminants in cultures which were perforce neglected for some time owing to pressure of work. Sufficient interest attaches to the remaining three, which were apparently incapable of inducing progressive tuberculosis in a guinea-pig, to warrant their consideration in relation to the radiological findings concerning the men who provided them.

The following notes refer to recruits from whose gastric content acid-fast bacilli were cultivated but proved non-virulent to guinea-pigs.

NUMBER 29.—The radiological report indicated soft mottling in the region of the first intercostal space on the right side with a possible cavity; there were old and healed tuberculous foci in the upper portion of the left lower lobe. A bacteriological examination of the gastric content was made. Discrete colonies of acid-fast bacilli were grown on each of three Petragnani tubes inoculated from the gastric mucus. A guinea-pig was inoculated by intraperitoneal injection with an emulsion prepared from a first subculture on July 26, 1940. No pigment production was observed in the discrete colonies of the primary cultures or in the confluent growths of the subcultures; the growths were smooth, soft and readily emulsifiable. The viability of the culture used for guinea-pig inoculation was shown by good growths in transplants made prior to the injection of the animal. The guinea-pig was killed on November 27, 1940, four months after inoculation. Autopsy revealed peritoneal adhesions of considerable strength and extent in the left upper quadrant of the abdomen; there were no tubercles on the peritoneum. The only visceral lesions apparent were small and sparsely distributed nodules in the lungs, of the size of a millet seed, but of doubtful nature. Microscopic examination of sections of the possible tubercles in the lungs revealed a histological structure which could not be reconciled with tuberculosis. The changes consisted of a small, round-celled reaction, limited by fibroblastic and fibrous tissue; there was no caseation or giant-cell formation. Attempts to demonstrate acid-fast bacilli in sections were unsuccessful.

NUMBER 41.—The radiological examination revealed no evidence of active tuberculosis, and the recruit was passed. Three tubes of Petragnani medium were inoculated from sputum and three from gastric content after preparation by the 6% sulphuric acid technique. No growth eventuated on any of the three tubes in which cultivation was attempted from the sputum, but a single colony of acid-fast bacilli appeared on one of the three tubes inoculated from the gastric content. A guinea-pig was inoculated by intraperitoneal injection with an emulsion of moderate density (one cubic centimetre) prepared from a well-covered tube obtained in the first subculture from the single colony; the growth was "smooth" lacked pigment, and emulsified readily. The guinea-pig was killed after the lapse of twelve weeks, but no lesions were discernible at the post-mortem examination. The culture used for inoculation proved viable.

NUMBER 97.—Radiological examination revealed apparent active pulmonary tuberculosis in the right upper lobe. The recruit was rejected. Good growths were obtained in primary cultures from the gastric content and colonies of macroscopic dimensions appeared after three weeks' incubation; they were ultimately pigmented, verrucose, "rough" and crumbly. Attempted emulsification in saline solution resulted in a lumpy suspension. A guinea-pig was inoculated on August 2, 1940, and killed on November 9, 1940. On post-mortem examination the animal displayed no pathological changes of any description; viability of the culture used for inoculation was shown by vigorous growth in subculture.

I am prepared to discard the acid-fast bacilli of gastric content cultures number 29 and number 41 as non-virulent saprophytes. The soldier represented by number 41 was passed radiologically; he was one of a number sent for bacteriological examination in error during a short period of confusion which prevailed in the early stages of the work. The acid-fast bacillus number 29 inflicted some tissue damage in the guinea-pig, as witness the peritoneal adhesions; it is doubtful if the small granulomata in the lungs were attributable to this microorganism, which might have been expected to provoke some "foreign-body" giant-cell reaction. In any event the histological characters did not suggest tuberculosis. An important consideration,

applicable to both number 29 and number 41, is that the bacterial growth in both cases was of that smooth, non-pigmented and easily emulsifiable character which distinguishes colonies of many acid-fast saprophytes from those of the "bread-crumb" pigmented colonies of *Mycobacterium tuberculosis* offering difficulty in the preparation of uniform suspensions in saline solution.

Although I have been compelled to reject cultures number 29 and number 41, it may be that they would have repaid further study. In one of a series of papers dealing with atypical acid-fast microorganisms, Max Pinner[15] describes acid-fast bacilli of "smooth" cultural characters, which he suggests may be smooth and relatively avirulent variants of human tubercle bacilli. His discussion is based on a study of four strains, three of which were cultivated from the morbid material of proved tuberculous foci; anomalous colonies providing the fourth strain arose in an old stock culture of the human type of *Mycobacterium tuberculosis* accidentally subjected to unfavourable conditions of incubation. The colonies of all four strains, as were those of my discarded number 29 and number 41, were round, dome-shaped and quite smooth, and when mixed with saline solution produced uniform bacterial suspensions. Virulence for laboratory animals was low, although the strains were not devoid of certain pathogenic properties. By means of serial animal passages Pinner was successful in effecting transformation of three of these strains into typical human tubercle bacilli. The resulting roughly growing colonies behaved in all respects like true human tubercle bacilli, their characteristics remaining stable in many generations of subcultures. Smooth and rough variants are known to exist in many bacterial species, and perhaps it is not too imaginative to suggest that some degree of instability in artificial culture may also be a property of tubercle bacilli. For these reasons, although I have rejected number 29 and number 41, I feel that it is possible that they were avirulent variants of *Mycobacterium tuberculosis*.

The decision to disallow culture number 97 was taken rather reluctantly in view of the positive radiological statement of active pulmonary tuberculosis and the cultural characters of the acid-fast bacillus—a verrucose, pigmented, glycerophilic strain, in rate of growth and general attributes an apparently typical example of the human type of *Mycobacterium tuberculosis*. In the absence of recognizable pathogenic effects in the guinea-pig it was held that the strain could not properly be included; but it is to be remembered that so long ago as 1910 Park and Krumweide[14] drew attention to the fact that the presence of tuberculosis may be doubtful on macroscopic examination of inoculated guinea-pigs, and indicated the necessity for cultural and further inoculation tests in such circumstances. In 1916 A. Eastwood and F. Griffith[13] appended a footnote to one of their papers, to the effect that tubercle bacilli of reduced virulence sometimes failed to reproduce macroscopic lesions in guinea-pigs, though the bacilli inoculated survived and were recoverable from apparently normal tissues. Relative to the probable existence of comparatively avirulent strains of *Mycobacterium tuberculosis*, Blacklock[12] cites the work of Sumiyoshi. In a study of the virulence of 30 strains of *Mycobacterium tuberculosis* isolated from sputum, Sumiyoshi found that two of them produced no lesions in guinea-pigs inoculated with emulsions of culture, while the other strains varied much in their virulence for the guinea-pig.

In the conditions under which the work forming the basis of this paper has been carried out, it has been impossible for me to undertake the further investigations indicated by the foregoing observations, but in excluding number 29, number 41 and number 97 from the total of cultures of *Mycobacterium tuberculosis* recovered from gastric content, I have felt that the last word has not been said about them.

## Conclusion.

The importance of directing attention to the contents of the fasting stomach in seeking bacteriological confirmation of a radiological diagnosis of pulmonary tuberculosis is cogently shown by the work of R. H. Stiehm,[16] director of the department of student health in the University of Wisconsin. Stiehm assembled 50 students in whom X-ray findings indicated the presence of what he termed "minimal" pulmonary lesions. In none of the group was there any clinical evidence of tuberculosis. All of the students regarded themselves as well, and in such samples of sputum as they could produce the tubercle bacillus could not be demonstrated. Acid-fast bacilli were observed in film preparations of the gastric mucus in nine instances; but in no less than 36 of the 50 (72%) tubercle bacilli were revealed in the gastric content by guinea-pig inoculation.

As showing the misleading nature of bacteriological findings based on the examination of sputum to the exclusion of gastric content, the figures obtained by Stiehm, in the study of persons concerning whom all indications pointed to active pulmonary disease, may be quoted. The methods of microscopic search and guinea-pig inoculation were applied to the gastric content in 48 of 71 such individuals, with the result that 43 (89·6%) were found to be discharging tubercle bacilli. By the examination of expectorated matter from 69 patients in the same group positive bacteriological findings were obtained in 10 instances only (14·5%). The same trend is to be observed in the work of Kane and Hounslow,[17] who by cultural methods and guinea-pig inoculation detected tubercle bacilli in the gastric content of 17 out of 55 sanatorium patients, who either produced no sputum or provided samples in which by identical procedures tubercle bacilli could not be demonstrated. The explanation of such discrepancies undoubtedly lies in the fact that many specimens submitted as sputum are of doubtful quality and do not represent genuine bronchial mucus.

The extension to the civilian community of routine thoracic radiography, now the order of the day in the services, will indicate bacteriological examination for many persons who will be found to have neither cough nor expectoration; for such people the best approach to laboratory confirmation of the existence of pulmonary tuberculosis is by way of the gastric content. The detection of tubercle bacilli in either sputum or gastric mucus not only establishes diagnosis, but indicates that the pulmonary lesion has not healed. In the management of declared sufferers from the disease who cannot supply sputum, or whose efforts in this direction result in the submission of scanty specimens of questionable nature, there is obvious scope for the bacteriological examination of gastric content as a guide in determining when those who have made apparently good clinical progress may be permitted to resume normal activities. It may seem a counsel of perfection; but that such permission should not be given until the gastric content has been shown repeatedly to harbour no tubercle bacilli is the logical conclusion.

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## ACTIVE IMMUNIZATION IN EXPERIMENTAL PERTUSSIS.

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BURNET AND TIMMINS[1] described an intranasal technique for infecting mice with *Hæmophilus pertussis* four years ago. Further, their work indicated that a significant degree of immunity against such infection could be demonstrated after intraperitoneal inoculation of living cultures or formolized vaccines. As a result of their findings they suggested that the method might be of value in the determination of the antigenic efficiency of vaccines prepared for the prophylaxis of whooping cough in children.

Most workers, however, still appear to favour other methods of infecting mice when conducting protection experiments. Culotta *et alii*[2] obtained inconclusive results with the intranasal method. They used a dose of 20,000 million organisms of Sauer's vaccine to protect mice. Their infecting dose was 400 million *Hæmophilus pertussis* organisms, and 50% of their control mice survived.

Miller and Silverberg,[3] Mishulow *et alii*[4] and Silverthorne[5] have all obtained satisfactory results in protection tests using the intraperitoneal route for infecting their mice. Miller and Silverberg[3] conceded, however, that the nasal route had the theoretical advantage of producing the infection in that part of the body where it naturally occurred. Nevertheless, they considered that the technical difficulties involved and the uncertainty of the killing dose outweighed the theoretical advantage over the intraperitoneal route.

The intranasal technique of infecting mice with *Hæmophilus pertussis* has been used in this laboratory over a period of years for investigating both passive[6][7] and active immunity. In view of the inconclusive results recorded by such workers as Culotta *et alii*[2] and Miller and Silverberg,[3] it seemed advisable first to extend Burnet and Timmins's observations by investigating the conditions under which protection could be regularly demonstrated with a "standard" reference vaccine. The results so obtained, together with those on the antigenic efficiency of vaccines prepared differently or stored under varying conditions, form the basis of this communication.

### Methods.

#### *Preparation of Vaccines.*

Growth from a 48-hour culture on Bordet-Gengou medium of a recently isolated strain of *Hæmophilus pertussis* showing Phase I characteristics was harvested in normal saline solution and centrifuged. From the deposit three batches of vaccine were prepared:

A. "Standard" vaccine: organisms suspended in saline solution containing 0·2% of "Tricresol" and 0·2% of phenol.

B. Formolized vaccine: organisms suspended in 0·2% formolized saline solution.

C. Heat-killed vaccine: organisms suspended in saline solution and placed in a water bath at 60° C. for one hour with no antiseptic.

All the vaccines were standardized to contain 10,000 million *Hæmophilus pertussis* organisms per cubic centimetre. Each of these vaccines was further divided into two parts. One part was stored in the cold-room at 0-4° C., the other in the incubator at 37° C. The "standard" vaccine stored in the cold room was used throughout in the preliminary work to determine the suitability of the method. The "standard" vaccine was not compared with the other vaccines until a period of at least four months in storage had elapsed.

The preparation of other vaccines used will be referred to as the experimental results are described.

#### *Administration of Vaccines.*

The mice were inoculated intraperitoneally, the vaccines being diluted with saline solution so that the volume given at any one injection was 0·5 cubic centimetre.

#### *Infection of Mice.*

The intranasal technique of infection described by Burnet and Timmins[1] has been used, 0·05 cubic centimetre of a suspension of living *Hæmophilus pertussis* being instilled into the nostrils of the mice under light general anæsthesia.

#### *Criteria of Immunity.*

Two criteria of immunity conferred by the administration of vaccines have been used.

1. Reduction of mortality in mice infected with a large dose of living Phase I *Hæmophilus pertussis* given intranasally. A dose of 50 million such organisms usually kills 80% to 100% of controls within a week. Doses as low as 5,000,000 *Hæmophilus pertussis* organisms may kill nearly as large a proportion of mice; but as the infecting dose is lowered the deaths are correspondingly delayed. When some immunity is present, but is insufficient to give protection against the infecting dose, deaths are delayed, a fact which may be utilized as another criterion of immunity.

2. Prevention of lung infection in mice given 5,000 to 50,000 living *Hæmophilus pertussis* organisms intranasally, doses producing a non-lethal infection in 80% or more of controls. The mice were killed with coal gas seven days after infection and the cut surface of the lower lobe of each lung was rubbed on a Bordet-Gengou plate. The plates were examined after three days' incubation and the degree of infection was graded arbitrarily as follows:

++++ = confluent growth.
+++ = semi-confluent growth.
++ = numerous discrete colonies (5 to 30 colonies per field of plate microscope magnification × 12).
+ = occasional colony.
O = no *Hæmophilus pertussis* colony.
C = contaminated lung culture—result discarded.

The results of both types of experiment have been evaluated statistically.

#### *Preparation of Suspensions.*

For the infecting suspension, growth from a 24-hour culture of Phase I *Hæmophilus pertussis* on a Bordet-Gengou slope was emulsified in nutrient broth. The bacterial content was then estimated by comparison with standard opacity tubes and the requisite dilutions were also made in nutrient broth. Colony counts of suitable dilutions on Bordet-Gengou medium gave figures which corresponded closely to the estimated bacterial content.

### Results.

#### *Protection Afforded by Standard Phase I Vaccine.*

It is recognized that protection against pertussis in human beings is partial rather than absolute after both artificial and natural active immunization.[6] It is therefore not surprising that difficulties may be experienced in demonstrating protection in mice if a suitable balance is not struck between the size of the infecting dose and the degree of immunity produced. The partial protection that follows a single intraperitoneal injection of vaccine is shown in Table I. It will be seen that a large dose of vaccine gives a highly significant protection against death when a moderate infecting dose—namely, 5,000,000

organisms—is used. As the immunizing dose is lowered, this protection is less definite, as reference to the table (Groups A, B, C and D) indicates. However, the benefit of the vaccine in even the smallest dose used is clearly shown by the freedom from infection in the survivors' lungs.

With a larger infecting dose of *Hæmophilus pertussis* (Groups E, F, G, H) no protection against death is apparent.

Repeated experiments carried out by us have shown (as in Table I) that significant protection against lethal doses of *Hæmophilus pertussis* can be produced by the giving of a single dose of vaccine. It seemed desirable, however, to determine whether better protection would be afforded if the doses of vaccine were spread over several injections. Most workers give more than one injection. Silverthorne[10] used five injections spread over a period of about four weeks.

We have not been able to demonstrate consistently higher protection in mice receiving multiple injections than in those receiving single injections of vaccine. The data of one of several such experiments against a large infecting dose are set out in Table II. It will be noted that the best protection is shown by mice in Groups B, C and F, which had respectively one, two and five injections. Group E mice, which received four injections, alone failed to show any definite protection against death, although in comparison with the control figures the increase in survival times is statistically highly significant.

The impression has been gained that the best immunity develops about a fortnight after injection of vaccine, and the fate of the mice in Groups A and B, though by itself not significant, tends to support this.

Immunity against small infecting doses of *Hæmophilus pertussis* is readily demonstrated by means of one or more doses of "standard" vaccine. Table III shows the results obtained in one such experiment. Reference to the table shows that the results with two injections of vaccine tend to be slightly better than those with one. However, the differences are not significant.

A further point of interest is the fact that a significant degree of protection can be demonstrated with a dose of vaccine containing as few as 10 million cells (Group H). In this case the protection is shown not by the number of mouse lungs specifically infected, but by a lessened intensity of infection as compared with the non-immunized controls. This dose for a mouse on a weight-for-weight basis corresponds with one of 5,000 million cells for a child weighing 10 kilograms (21 pounds). Although caution must be exercised in the application of the results of these mouse experiments to the case of humans, they tend to support Vickery's[12] contention that Phase I pertussis vaccine in doses of 30,000 million to 40,000 million organisms will give protection against whooping cough to a very large percentage of children.

The results obtained by the large and the small infecting dose methods are compared in Figure I. Curve A is obtained by plotting the percentage of survivors in Groups A, B, C and D (Table I) against the logarithm of the dose of vaccine. In Curve B the percentage of specifically infected lungs (Table III) is likewise plotted against the logarithm of the vaccine dosage.

TABLE I.

*Protective Action of "Standard" Hæmophilus pertussis Vaccine against Intranasal Infecting Doses of Hæmophilus pertussis.*[1]

| Group of Mice. | Dose of Vaccine in Millions of Organisms. | Infecting Dose in Millions of Organisms. | Number of Deaths. | Day of Death. | Intensity of Infection in Survivors' Lungs.[2] | Number of Survivors' Lungs Specifically Infected. | Statistical Significance Compared with Untreated Controls. | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Of Number of Deaths. | Of Number of Specifically Infected Lungs of Survivors. |
| A | 1,000 | 5 | 0/15 | | 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0 | 0/15 | $P$[3]=0·0032 | $P$=0·00000204 |
| B | 500 | 5 | 3/15 | 3, 4, 5 | +, +, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, C | 1/11 | $P$=0·122 | $P$=0·000012 |
| C | 100 | 5 | 5/13 | 3, 4, 5, 6, 6 | 0, 0, 0, 0, 0, 0, 0, C | 0/7 | $P$=0·48 | $P$=0·00015 |
| D | Nil (controls) | 5 | 7/15 | 3, 3, 3, 4, 5, 11, 17 | +++, +++, +++, +++, +++, +++, + | 8/8 | | |
| E | 1,000 | 50 | 15/15 | 2, 2, 2, 2, 2, 2, 2, 3, 3, 3, 3, 3, 3, 7 | | | | |
| F | 500 | 50 | 15/15 | 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 3, 3, 3, 4 | | | | |
| G | 100 | 50 | 14/15 | 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 3 | 0 | 0/1 | | |
| H | Nil (controls) | 50 | 14/14 | 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 3 | | | | |

[1] Mice infected intranasally 15 days after Groups A, B, C, E, F and G received vaccine in a single dose.
[2] The survivors were killed 21 days after the infecting dose and the lungs were inoculated on to nutrient media.
[3] $P$=probability factor. When $P$=0·01 the odds are 1 in 100 that the result obtained is due to chance. Values of 0·05 or less are regarded as statistically significant, and values of 0·005 or less highly significant.

TABLE II.

*Protection Afforded by a Constant Amount of "Standard" Hæmophilus pertussis Vaccine when Administered in Varying Numbers of Injections.*[1]

| Group of Mice. | Total Dosage of Vaccine in Millions of Organisms. | Number of Injections. | Interval between Final Injection of Vaccine and Infecting Dose. | Number of Mice Alive 28 Days After Infection. | Day of Death. | Statistical Significance of Survivals Compared with Untreated Controls. |
|---|---|---|---|---|---|---|
| A | 1,000 | 1 | 29 | 5/20 | 1, 2, 2, 2, 2, 2, 2, 2, 3, 3, 3, 3, 3, 4, 4, 4 | $P$=0·024 |
| B | 1,000 | 1 | 15 | 9/20 | 2, 2, 2, 3, 4, 4, 5, 6, 6, 6, 14 | $P$=0·00061 |
| C | 1,000 | 2 | 15 | 8/18 | 3, 4, 4, 4, 4, 5, 6, 6, 8, 8 | $P$=0·00089 |
| D | 1,000 | 3 | 15 | 5/17 | 3, 3, 3, 3, 3, 3, 4, 4, 4, 6, 9, 12 | $P$=0·014 |
| E | 1,000 | 4 | 15 | 2/19 | 2, 3, 3, 3, 3, 3, 3, 4, 4, 4, 4, 4, 4, 5, 5, 9, 21 | $P$=0·23[2] |
| F | 1,000 | 5 | 15 | 7/15 | 3, 3, 3, 4, 4, 5, 6, 18 | $P$=0·00096 |
| G | Nil (controls) | Nil | — | 0/20 | 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 3, 3, 8 | |

[1] Immunization of the groups of mice was commenced on different days, so that the final dose in Groups B to F was administered the same day. All mice were infected with 50 million *Hæmophilus pertussis* organisms intranasally on the one day.
[2] Not significant, but survival times show a significant difference; $P$ is considerably less than 0·001.

It will be seen that use of the small infecting dose technique enables smaller amounts of specific antibody to be detected than does the large infecting dose technique. Curve B is much steeper than Curve A. This in effect means greater sensitivity as a method of assay.

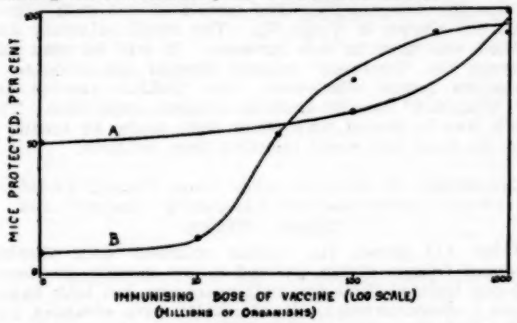


FIGURE I.
Curve A shows the percentage of survivors following a large infecting dose among groups of mice immunized with different quantities of vaccine. Curve B shows the percentage of animals with lungs free of organisms seven days after a small infecting dose among groups of mice immunized with different quantities of vaccine.

These results indicate that (*a*) significant protection can be demonstrated against subsequent specific intranasal infection, by means of a single injection of vaccine intraperitoneally, and (*b*) greater sensitivity in the detection of immunity is provided by the technique employing a small as opposed to a large infecting (or lethal) dose of *Hæmophilus pertussis*.

From the practical standpoint there are certain advantages in giving the test mice only one injection of vaccine. The length of time required for the completion of experiments is lessened, likewise the risk of non-specific deaths from intercurrent disease. Again, it has been often noticed that large and especially repeated intraperitoneal injections of a potent pertussis vaccine impair the general health and nutrition of the mice. The probable cause of this ill health will be discussed later. Mice vaccinated subcutaneously were found to remain in good health, but they did not appear to develop such good specific immunity.

For these reasons it was decided to adhere to a single injection of vaccine in experiments in which the antigenic efficiency of different vaccines was being measured.

### *Comparison of Antigenicity of Vaccines Killed by Different Means and Stored at Different Temperatures.*

Tests were first made with Phase I vaccines sterilized by (*a*) cresol and phenol, (*b*) formol saline solution, and (*c*) heat, respectively, and stored at 0° C. and 37° C. By means of the large infecting dose as a method of assay, protection was shown with all these vaccines. The impression was gained that antigenicity was impaired by storage at 37° C., but the results generally were inconclusive, especially as regards the most suitable method of sterilizing the vaccines.

TABLE III.
*Protection Afforded by "Standard"* Hæmophilus pertussis *Vaccine against Small Infecting Doses of* Hæmophilus pertussis.[1]

| Group of Mice. | Total Dosage of Vaccine in Millions of Organisms. | Number of Injections. | Intensity of Mouse Lung Infection. | Number of Specifically Infected Lungs. | Statistical Significance of Number of Infected Lungs Compared with Untreated Controls. |
|---|---|---|---|---|---|
| A | 1,000 | 1 | +++, ++, +, 0, 0, 0, 0, 0, 0, 0, 0, 0, C | 3/12 | $P=0·00058$ |
| B | 1,000 | 2 | +, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, C, C | 1/11 | $P=0·000035$ |
| C | 330 | 1 | +++, +, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, C | 2/13 | $P=0·00006$ |
| D | 330 | 2 | +, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, C, C | 1/13 | $P=0·000009$ |
| E | 100 | 1 | ++, ++, ++, +, +, 0, 0, 0, 0, 0, 0, 0, 0 | 5/13 | $P=0·004$ |
| F | 100 | 2 | +, +, +, +, 0, 0, 0, 0, 0, 0, 0, 0, 0, | 4/15 | $P=0·00037$ |
| G | 33 | 2 | ++++, ++, ++, ++, +, +, +, +, 0, 0, 0, 0, 0, 0, 0 | 7/15 | $P=0·0095$ |
| H | 10 | 2 | ++++, ++++, +++, +++, +++, +++, ++, ++, +, +, +, +, 0, 0 | 13/15 | $P=0·5148$[2] |
| J | Nil (controls) | Nil | ++++, ++++, ++++, ++++, ++++, ++++, ++++, +++, +++, +++, +++, ++, ++, 0, C | 13/14 | |

[1] Mice in Groups B, D, F, G and H received a second injection of vaccine (seven days after their first dose) on the same day as Groups A, C and E received their single injection. All mice were infected intranasally with 5,000 *Hæmophilus pertussis* organisms fifteen days later and killed and the lungs were plated after a further seven days.
[2] Although there is no significant reduction in number of infected lungs, there is a significant lessening of intensity of infection ($P=0·048$).

TABLE IV.
*The Effect on Antigenicity of* Hæmophilus pertussis *Vaccines of Varying Storage Temperature, and Methods of Killing the Organisms.*[1]

| Group of Mice. | Method of Sterilization. | Storage Temperature. | Intensity of Mouse Lung Infection. | Number of Specifically Infected Lungs. | Statistical Significance Compared with Untreated Controls. |
|---|---|---|---|---|---|
| A | "Tricresol" and phenol, each 0·2%. | 0° C. | ++, +, +, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, C, C | 3/20 | $P=0·000000013$ |
| B | | 37° C. | ++++, ++, +, +, +, +, +, +, +, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, C | 9/24 | $P=0·0000049$ |
| C | Formol saline solution, 0·2%. | 0° C. | ++++, +++, +++, ++, ++, ++, +, +, +, +, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, C | 10/22 | $P=0·000058$ |
| D | | 37° C. | ++++, +++, +++, ++, ++, +, +, +, +, +, +, +, +, +, 0, 0, 0, 0, 0, 0, 0, C, C, C | 14/21 | $P=0·0052$ |
| E | Heat killed, at 60° C. for one hour. | 0° C. | ++++, ++, ++, +, +, +, +, +, +, +, 0, 0, 0, 0, 0, 0, 0, 0, 0, C, C | 10/22 | $P=0·000058$ |
| F | | 37° C. | ++++, ++++, ++++, ++++, ++++, +++, +++, +++, +++, ++, ++, ++, ++, ++, +, +, +, +, 0, 0, 0, 0, 0, 0 | 19/25 | $P=0·022$ |
| G | Controls. | — | ++++, ++++, ++++, ++++, ++++, ++++, ++++, ++++, ++++, ++++, ++++, ++++, ++++, ++++, ++++, +++, +++, +++, C | 20/20 | |

[1] All mice infected with 5,000 *Hæmophilus pertussis* organisms intranasally 16 days after Groups A to F had received a single injection of vaccine containing 1,000 million *Hæmophilus pertussis* organisms, sterilized and stored as shown in the second and third columns. The mice were killed and the lungs were inoculated on to nutrient media seven days after infection.

The more sensitive technique, employing small non-lethal infecting doses, gave much more useful information. The data of one such experiment are shown in Table IV. It will be noticed that all the vaccines give a significant degree of immunity. Of those stored at 0° C. the formolized and heat-killed products give an equal amount of protection, whilst the vaccine killed with "Tricresol" and phenol shows a highly significant advantage over both of them ($P = 0.0017$). Further, it is seen that in each case the vaccines stored at 0° C. (Groups A, C and E) afforded better protection than the corresponding products kept at 37° C. (Groups B, D and F). The combined results are statistically significant in favour of cold-room storage ($P = 0.016$).

*Hæmophilus pertussis* is easily killed by heat, a temperature of 56° C. for six minutes proving fatal. Heat-killing at 60° C. for sixty minutes impairs the antigenicity, as shown above. Tested against a large infecting dose, a vaccine in which the *Hæmophilus pertussis* was killed by heating at 56° C. for eight minutes, gave interesting results compared with one containing "Tricresol" and phenol. The data of such an experiment are shown in Table V. All immunized groups of mice in the test except those in Group F, which received the least amount of heat-killed vaccine, showed significant protection. However, as the dose of heat-killed vaccine was increased, the immunity correspondingly increased. With the cresol and phenol-killed vaccine the degree of immunity did not run parallel with an increase of the dose; the mice receiving the smallest dose (Group E) showed better protection than those receiving the largest amount (Group A). Possible reasons for these irregular results will be discussed later.

When the small infecting dose technique was used, complete protection against mouse lung infection was given by both vaccines in doses of 100 million organisms. Smaller doses were not tried.

### *Comparison of "Standard" Vaccine with Commercial Pertussis Vaccines.*

Samples of pertussis (Phase I) vaccine prepared locally ("C.S.L.") and a product described as a "highly concentrated and detoxicated whooping cough vaccine", prepared overseas ("overseas") were obtained. The latter was stated to contain 20,000 million organisms per cubic centimetre. Several experiments were carried out in which these commercial products have been compared with the "standard" vaccine for antigenicity. The results of one such experiment are shown in Table VI. The small infecting dose method was used in this instance. It will be seen that whereas the "overseas" vaccine showed no evidence of protective power whatosever, the "C.S.L." vaccine and our "standard" vaccine afforded complete protection. This result was in accord with other tests made, by means of both the large and small infecting dose methods.

### *Comparison of Vaccines made from Freshly Isolated Phase I Strain and Old Laboratory "Smooth" and "Rough" Strains.*

Table VII shows the results obtained with vaccines prepared from a strain isolated a few months previously and one isolated three and half years ago, but both having Phase I characteristics. Good results were obtained with both vaccines in doses of 100 million organisms, and there is no significant difference between Groups A and B. The same uniformity of results was found with other corresponding doses of the vaccines.

In the case of the vaccine prepared from the "rough" strain, no definite protection against death was shown with doses as high as 1,000 million organisms. When it was tested by the method using small non-killing doses of living *Hæmophilus pertussis* some degree of protection was shown. Compared, however, with a potent Phase I vaccine, its antigenicity is very small.

## Discussion.

The results reported in this paper confirm Burnet and Timmins's[2] findings that a significant degree of immunity against intranasal *Hæmophilus pertussis* infections in mice can be demonstrated after an intraperitoneal inoculation of vaccine. Further, it has been shown that the method is of value in determining the comparative values of different vaccines.

TABLE V.

*Comparison of a Minimal-heat-killed Vaccine with One Sterilized with "Tricresol" and Phenol against a Large Infecting Dose of* Hæmophilus pertussis.[1]

| Group of Mice. | Method of Preparing Vaccine. | Dose of Vaccine in Millions of Organisms. | Number of Survivors 28 Days after Infection. | Day of Death. | Statistical Significance Compared with Untreated Controls. |
|---|---|---|---|---|---|
| A | T. and P.[2] | 1,000 | 8/15 | 3, 7, 7, 8, 8, 9, 13 | $P=0.0251$ |
| B | Heat.[2] | 1,000 | 11/14 | 9, 17, 19 | $P=0.00058$ |
| C | T. and P. | 330 | 7/13 | 2, 4, 4, 4, 5, 6 | $P=0.029$ |
| D | Heat. | 330 | 11/15 | 2, 3, 4, 5 | $P=0.00125$ |
| E | T. and P. | 100 | 10/15 | 3, 3, 6, 8, 10 | $P=0.00382$ |
| F | Heat. | 100 | 3/15 | 2, 2, 2, 2, 2, 2, 3, 3, 3, 4, 4, 5 | $P=0.5$ |
| G | Controls. | Nil | 2/15 | 2, 2, 2, 3, 3, 4, 5, 5, 6, 7, 7, 8, 11 | |

[1] All groups of mice were infected intranasally with 50 million *Hæmophilus pertussis* organisms 16 days after Groups A to F received a single injection of vaccine.

[2] Vaccines prepared from the same harvest of *Hæmophilus pertussis*. T. and P.—organisms suspended in a solution of "Tricresol" and phenol, each 0·2%. Heat—heated at 56° C. for eight minutes and tested for sterility. Both lots of vaccines were stored in the cold room for four days before use.

TABLE VI.

*Comparison of Antigenicity of Commercial and "Standard" Vaccines.*[1]

| Name of Vaccine. | Dosage of Vaccine in Millions of Organisms. | Intensity of Mouse Lung Infection. | Number of Specifically Infected Mouse Lungs. | Statistical Significance Compared with Untreated Controls. |
|---|---|---|---|---|
| "Overseas"[2] .. | 1,000 | +++, +++, +++, ++, ++, +, +, +, +, 0, 0, 0, C | 11/14 | None |
| "C.S.L."[3] .. | 1,000 | 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0 | 0/15 | $P=0.000000236$ |
| "Standard"[4] .. | 1,000 | 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0 | 0/15 | $P=0.000000236$ |
| —— | Nil (controls) | +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +++, +, +, +, +, 0, 0, 0, 0, 0, 0, C | 23/29 | |

[1] Treated groups of mice received the vaccine in one injection, and all mice were infected intranasally 15 days later with 50,000 *Hæmophilus pertussis* organisms. The mice were killed after a further seven days and the lungs were inoculated on to nutrient media.

[2] "Overseas"—commercial "highly concentrated and detoxicated whooping cough vaccine" prepared overseas.

[3] "C.S.L."—stock Pertussis (Phase I) Vaccine.

[4] "Standard"—reference vaccine, preparation described in text.

TABLE VII.

*Comparison of Antigenicity of Vaccines Prepared from "Smooth" and "Rough" Strains of* Hæmophilus pertussis.[1]

| Group of Mice. | Name of Vaccine. | Dose of Vaccine in Millions of Organisms. | Number of Survivors 28 Days After Infection. | Day of Death. | Statistical Significance Compared with Untreated Controls (E). |
|---|---|---|---|---|---|
| A | "Fresh smooth."[2] | 100 | 9/16 | 3, 7, 7, 7, 13, 14, 22 | $P=0{\cdot}00297$ |
| B | "Old smooth."[3] | 100 | 11/16 | 7, 7, 7, 8, 12 | $P=0{\cdot}000317$ |
| C | "Rough."[4] | 1,000 | 2/16 | 4, 4, 6, 7, 7, 7, 8, 8, 8, 9, 9, 10, 10, 11 | $P=0{\cdot}5$ |
| D | "Rough."[4] | 100 | 3/15 | 3, 3, 5, 5, 6, 7, 7, 7, 9, 10, 12, 14 | $P=0{\cdot}28$ |
| E | — | Nil (controls) | 1/16 | 1, 5, 5, 5, 6, 6, 6, 7, 7, 7, 8, 8, 10, 13, 18 | |

[1] Mice in Groups A, B, C and D received vaccine in one injection. All mice were infected intranasally with 25 million *Hæmophilus pertussis* organisms (fresh "smooth" strain) 16 days later. The significance of the results is further referred to in the text.
[2] Fresh "smooth" = vaccine prepared from recently isolated strain.
[3] Old "smooth" = vaccine prepared from strain isolated three and a half years previously, but maintaining Phase I characteristics. Both "fresh" and old "smooth" vaccines were prepared under identical conditions and stored together in the cold room.
[4] "Rough" = vaccine prepared from "rough" strain (in Phase III) maintained on serum agar for years. Vaccine was prepared on the same day and stored with "smooth" vaccines.

Our results indicate that "Tricresol" and phenol are satisfactory for sterilizing and preserving pertussis vaccines. The antigenicity was found to be impaired by storage at 37° C. as compared with that of vaccine stored in the cold-room. It would therefore be wise, when active immunization is contemplated, for the vaccine to be used as soon as possible after being received from the makers or from a suitable storage depot.

The observations recorded in Table VII call for special comment. They confirm the generally accepted view that an antigenically efficient vaccine must be prepared from Phase I *Hæmophilus pertussis*. They also show that it is not necessary to use a culture only recently isolated from a case of pertussis to prepare a satisfactory vaccine. What is necessary is that the culture should retain its Phase I characteristics, and this it may do for years if suitably maintained. If it were essential to use only strains isolated within a period of a few weeks or months from a case of whooping cough, it would be most difficult for a manufacturing laboratory to build up adequate stocks of potent vaccine during an inter-epidemic period.

It is interesting to find that by the use of these methods of assay the same general conclusion as to the relative efficiency of pertussis antigens has been reached as by workers using the intraperitoneal route of infection.[(3)(5)(8)(10)] It is not, however, perfectly clear why the results should agree so closely.

Leslie and Gardner's[(11)] observations support Bordet's view that when intraperitoneal injections of living cultures of *Hæmophilus pertussis* are given to test animals, death is purely toxic in nature. If this view is correct, the intraperitoneal route of infection after the administration of vaccine is a measure of antitoxic rather than of antibacterial immunity. The criterion of immunity in our small infecting dose method of assay has been the prevention or lessening of lung infection in vaccinated mice. This must be regarded as a measure of antibacterial and not antitoxic power.

It is uncertain whether antitoxic immunity plays any part in overcoming whooping cough in humans. For this reason and because of its relative sensitivity in measuring small variations in antigenicity, this technique has definite advantages. As Miller and Silverberg[(3)] state, the nasal route has the theoretical advantage of producing the infection in that part of the body where it naturally occurs. We would also point out that the nature of the lesions in the respiratory tract in the mouse bears some resemblance to the lesions in humans; the lesions produced after intraperitoneal infection are practically identical with those produced by the injection of pertussis endotoxin.

The harmful effect of large intraperitoneal injections of vaccine on the health of the mice has already been referred to. As a result of unpublished observations, we believe that the effect is due to pertussis endotoxin and that the results shown in Table V may be explained on this basis. Heating impairs the antigenicity of the vaccine and also destroys or alters the endotoxin. A large dose of the vaccine, therefore, is necessary to afford significant protection, but is not toxic for the mice. The cresol-killed vaccine, which was prepared only four days before use in this particular experiment, still contained a considerable amount of unaltered endotoxin. Moderate doses give good immunity; but any increase in the specific immunity by the administration of greater amounts of vaccine is at least counterbalanced by the less satisfactory general health of the mice caused by the larger dose of endotoxin.

## Summary and Conclusions.

1. The intranasal technique of Burnet and Timmins has been used for measuring the antigenic efficiency of pertussis vaccines in mice.

2. A large (lethal) and a small (non-lethal) infecting dose method for assay of antigenicity have been compared.

3. The advantages of the small infecting dose method have been shown.

4. Vaccines killed with cresol or with cresol and phenol proved better antigenically than formolized or heat-killed vaccines.

5. Storage at a low temperature is necessary to preserve full antigenic efficiency.

6. An antigenically efficient vaccine may be prepared from a strain of *Hæmophilus pertussis* "not recently isolated", provided it maintains its Phase I characteristics.

7. Little protection was afforded by a vaccine prepared from a "rough" (Phase III) strain.

8. A commercial "detoxicated" pertussis vaccine failed to show any antigenicity.

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# THE FAILURE OF TREATMENT WITH PLACENTA, WITH VITAMIN C AND WITH "PRONTOSIL" IN CHRONIC MYELOID LEUCHÆMIA.

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## TREATMENT WITH PLACENTA.

THE literature of leuchæmia is full of reports of experimental treatment of patients suffering from chronic leuchæmia with endocrine products or extracts of organs of animals. These experiments were conducted on the hypothesis that leuchæmia is a disease caused by an insufficiency or dysfunction of the glands of internal secretion.

Forkner gives a summary of these papers on pages 235 and 236 of his monograph about leuchæmias, to which I refer here in order to save space. Hitherto all these experiments have failed to produce positive results which could stand a critical reexamination, and there is no proof that medication with extracts or whole organs, such as spleen, thymus, lymph glands, bone marrow or pancreas, or with fresh fœtal extracts, is of any value as treatment in cases of leuchæmia.

According to the work of Schmidt, Schridde, Naegeli and Maximow, it is generally accepted that the changes of chronic myeloid leuchæmia resemble closely special stages of the embryonic blood formation in their localization and morphology. One speaks practically of a reawakening in leuchæmia of the areas of the embryonic blood formation in liver, spleen and kidney. Especially Naegeli and his school postulate further investigation into endocrine disturbances in cases of leuchæmia, which they believe are the real cause of the disease.

Assuming that under normal conditions the placenta has a large hormonal influence on the fœtus and also on its blood formation, and assuming that under normal conditions the placenta also contributes to the involution of the foci of hæmatogenesis in the liver, spleen, kidney *et cetera* in the later months of pregnancy (as it were, helps to remove the leuchæmic state of the embryo), I tried medication with placenta in cases of chronic leuchæmia.

Two patients with chronic leuchæmia were fed for thirty days with mature fresh placenta. The patients each

TABLE I.[1]

*Case I.*

| Time of Estimation. | Leucocytes per Cubic Millimetre. | Polymorphonuclear Cells. (Percentage.) | Myelocytes. (Percentage.) | Myeloblasts. (Percentage.) | Lymphocytes. (Percentage.) | Nucleated Red Cells. | Hæmoglobin Value. (Sahli.) |
|---|---|---|---|---|---|---|---|
| Before placental meals .. .. .. | 112,000 | 70 | 20 | 10 | — | Present. | 60 |
| First day .. .. .. .. .. | 102,000 | 70 | 23 | 6 | 1 | Present. | 60 |
| Tenth day .. .. .. .. .. | 120,000 | 64 | 26 | 8 | — | Present. | 60 |
| Twentieth day .. .. .. .. | 156,000 | 64 | 27 | 9 | — | Present. | 62 |
| Thirtieth day .. .. .. .. .. | 215,000 | 72 | 21 | 6 | — | Present. | 65 |

TABLE II.

*Case II.*

| Time of Estimation. | Leucocytes per Cubic Millimetre. | Polymorphonuclear Cells. (Percentage.) | Myelocytes. (Percentage.) | Myeloblasts. (Percentage.) | Lymphocytes. (Percentage.) | Nucleated Red Cells. (Percentage.) | Hæmoglobin Value. (Sahli. |
|---|---|---|---|---|---|---|---|
| Before placental meals .. .. .. | 91,000 | 70 | 29 | Present | — | Present | 90 |
| Tenth day .. .. .. .. .. | 141,000 | 52 | 43 | 3 | 1 | 1 | — |
| Twentieth day .. .. .. .. .. | 165,000 | 48 | 43 | 7 | 1 | 1 | 88 |
| Thirtieth day .. .. .. .. .. | 195,000 | 42 | 48 | 8 | 1 | 1 | — |

[1] Blood for the counts was obtained by venepuncture; in the differential count on films 200 cells were counted for each 10,000 leucocytes.

TABLE III

*Treatment with 200 Milligrammes per Day of Vitamin C, given Intravenously: Results of Blood Counts*

| Patient. | Sex. | Age. (Years.) | Clinical Condition. | Time of Blood Count. | Leucocytes per Cubic Millimetre. | Polymorphonuclear Cells. (Percentage.) | Myelocytes. (Percentage.) | Myeloclasts. (Percentage.) | Eosinophile Cells. (Percentage.) | Basophile Cells. (Percentage.) | Nucleated Red Cells. (Percentage.) | Erythrocytes per Cubic Millimetre. | Hæmoglobin. (Grammes *per Centum*.) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| M. | F. | 43 | Chronic myeloid leuchæmia of one year's duration, general enlargement of all lymph glands, spleen and liver. | Before treatment .. | 160,000 | 44 | 46 | 2 | 2 | 6 | Present | 3,450,000 | 9·67 |
| | | | | First day .. | 261,000 | 37 | 56 | 2 | 1 | 3 | Present | | |
| | | | | Third day | 356,000 | 31 | 59 | 4 | 3 | 3 | | | |
| | | | | Sixth day .. | 210,000 | 55 | 26 | 6 | 1 | 2 | | | |
| | | | | Eighth day (Therapy interrupted.) | 380,000 | 42 | 50 | 2 | 2 | 2 | 1 | 3,350,000 | 8·89 |
| A.N | M. | 37 | Chronic myeloid leuchæmia for three years, enlarged liver and spleen, spleen reaching to umbilicus. | Before treatment .. | 70,000 | 41 | 35 | 12 | Present. | 12 | Present. | 4,700,000 | 12·63 |
| | | | | First day .. | 82,000 | 36 | 37 | 9 | 3 | 15 | Present. | | |
| | | | | Fifth day .. | 81,000 | 48 | 25 | 11 | 5 | 11 | Present. | | |
| | | | | Tenth day .. | 64,500 | 54 | 22 | 7 | 3 | 13 | Present. | 3,240,000 | 11·23 |
| O.D | M. | 40 | Chronic myeloid leuchæmia for twenty months, enlarged liver and spleen. | Before treatment .. | 119,000 | 47 | 47 | 2 | 4 | — | Present. | 4,500,000 | 13·26 |
| | | | | First day .. | 125,000 | | | | | | | | |
| | | | | Fifth day .. | 110,000 | 59 | 32 | 4 | 1 | 4 | Present. | | |
| | | | | Tenth day .. | 131,000 | 49 | 45 | 3 | Present. | 3 | Present. | 3,700,000 | 11·8 |

received daily by mouth one mature fresh placenta of approximately 400 to 500 grammes in weight. The blood was examined daily before the placental meal. The placentæ were kept fresh on ice and were minced directly before the meal, and the taste was improved with sugar and chocolate. After fourteen days of continuous fresh placental meals, carefully dried and pulverized placenta was given according to our supply of placenta (the placentæ were dried at 37° C. in a special drying oven originally used for the preparation of insulin from fresh pancreas). After thirty days of continuous placental feeding the experiment was terminated because no improvement was observed.

### Reports of Cases.

CASE I.—A male patient, aged thirty-four years, had suffered from chronic myeloid leuchæmia for fifteen months. He had enlargement of the spleen and achlorhydria. The last course of deep X-ray therapy was completed two months before the commencement of the placental meals. In order to enable the patient to digest the placenta, from the seventh

TABLE IV.
*Treatment with "Prontosil". Results of Blood Counts.*

| Patient. | Sex. | Age. (Years.) | Clinical Condition. | Time of Treatment. | Hæmoglobin. (Grammes per 100 Cubic Centimetres.) | Erythrocytes per Cubic Millimetre. | Leucocytes per Cubic Millimetre. | Myeloblasts. (Percentage.) | Myelocytes. (Percentage.) | Polymorphonuclear Cells. (Percentage.) | Monocytes. (Percentage.) | Nucleated Red Cells. (Percentage.) | Platelets. | Lymphocytes. (Percentage.) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A.E.N. | M. | 35 | Chronic myeloid leuchæmia. | One month before treatment .. | 13·8 | 5,200,000 | 42,000 | 5 | 25 | 63 | — | Present | Plentiful | 5 |
| | | | | Day of treatment before first dose | 12·1 | 4,300,000 | 54,000 | 13 | 30 | 54 | — | Present | Plentiful | 3 |
| | | | | First day .. | 12·9 | 4,500,000 | 63,000 | 6 | 21 | 72 | — | Present | Plentiful | 1 |
| | | | | Second day .. | 13·1 | 6,500,000 | 51,000 | 6 | 18 | 74 | — | Present | Plentiful | 2 |
| | | | | Third day .. | 13·4 | 4,700,000 | 81,000 | 7 | 25 | 67 | — | Present | Plentiful | 1 |
| | | | | Fourth day .. | 12·1 | 4,200,000 | 52,000 | 3 | 18 | 77 | — | Present | Plentiful | 2 |
| | | | | Ten days after treatment .. | 13·4 | 4,800,000 | 70,000 | 11 | 36 | 52 | — | Present | Normal | 1 |
| R.P. | F. | 40 | Chronic myeloid leuchæmia. | One month before treatment .. | 11·3 | 4,300,000 | 79,000 | 1 | 26 | 68 | 1 | 1 | — | 3 |
| | | | | Day before first dose .. .. | 12·9 | 4,000,000 | 90,000 | 2 | 18 | 77 | — | 1 | Present | 2 |
| | | | | First day .. | 12·8 | — | 64,000 | 1 | 22 | 77 | — | Present | Normal | — |
| | | | | Second day .. | 11·2 | — | 59,000 | 1 | 23 | 74 | — | 1 | Normal | 1 |
| | | | | Third day .. | 10·9 | 3,900,000 | 60,000 | 1 | 21 | 77 | — | Present | Normal | 1 |
| | | | | Fourth day .. | 13·2 | 4,700,000 | 67,000 | 2 | 38 | 59 | — | Present | Normal | 1 |
| | | | | Fifth day .. | 11·2 | 3,900,000 | 75,000 | 1 | 32 | 67 | — | Present | Normal | Present |
| | | | | Ten days after treatment .. | 12·8 | 4,800,000 | 74,000 | 2 | 32 | 64 | — | 1 | Plentiful | 1 |
| J.O'D. | M. | 45 | Chronic myeloid leuchæmia. | One month before treatment .. | 16·2 | 5,600,000 | 40,000 | 1 | 21 | 74 | 1 | 3 | — | 1 |
| | | | | Day before first dose .. | 16·3 | — | 70,000 | 4 | 20 | 75 | — | 1 | Normal | Present |
| | | | | First day .. | 15·1 | 5,400,000 | 66,000 | 2 | 16 | 81 | — | 1 | Normal | Present |
| | | | | Second day .. | 13·8 | 5,600,000 | 80,000 | 1 | 17 | 81 | — | 1 | Decreased | Present |
| | | | | Third day .. | 14·3 | 5,600,000 | 99,000 | 1 | 24 | 75 | — | Present | Normal | Present |
| | | | | Fourth day .. | 13·4 | 5,200,000 | 86,000 | 1 | 19 | 78 | — | Present | Plentiful | 2 |
| | | | | Fifth day .. | 14·0 | 4,800,000 | 116,000 | 3 | 21 | 73 | — | 2 | Normal | 1 |
| | | | | Ten days after treatment .. | 13·1 | 4,100,000 | 114,000 | 2 | 21 | 74 | — | 2 | Normal | 1 |
| R.B.[1] | M. | 54 | Acute myeloid leuchæmia | One month before treatment .. | 9·2 | 2,800,000 | 45,000 | 34 | 6 | 47 | 7 | — | 6 | Scanty. |
| | | | | Day before first dose .. .. | 12·0 | 3,400,000 | 75,000 | 38 | 6 | 48 | 8 | — | Present | Scanty |
| | | | | First day .. | 10·9 | 4,000,000 | 68,000 | 24 | 11 | 46 | 17 | — | 2 | Scanty |
| | | | | Second day .. | 11·2 | — | 70,000 | 46 | 4 | 40 | 8 | — | 2 | Scanty |
| | | | | Third day .. | 11·5 | 2,800,000 | 86,000 | 39 | 6 | 43 | 11 | — | 1 | Scanty |
| | | | | Fourth day .. | 10·9 | 3,900,000 | 80,000 | 50 | 7 | 34 | 7 | — | 2 | Scanty |
| | | | | Fifth day .. | 10·9 | 3,700,000 | 85,000 | 48 | 12 | 32 | 7 | — | 1 | Scanty |
| | | | | Sixth day .. | 10·1 | 3,200,000 | 74,000 | 44 | 13 | 34 | 7 | — | 2 | Scanty |
| | | | | End of "Prontosil" | 9·3 | 2,900,000 | 166,000 | 59 | 12 | 28 | — | — | 1 | Scanty |
| M.W.[1] | F. | 40 | Acute myeloid leuchæmia. | Three days before treatment .. | 12·0 | 4,310,000 | 130,000 | 78 | 12 | 4 | 6 | — | — | Scanty |
| | | | | Two days before treatment .. | 10·9 | 3,700,000 | 267,000 | 92 | 5 | 3 | — | — | Present | Scanty |
| | | | | First day .. | 10·1 | 3,100,000 | 262,000 | 93 | 4 | 2 | 1 | — | Present | Scanty |
| | | | | Second day .. | 7·8 | 2,700,000 | 290,000 | 95 | 2 | 3 | — | — | Present | Scanty |
| | | | | Third day .. | — | 2,200,000 | 287,000 | 97 | 2 | 1 | — | — | Present | Scanty |
| | | | | Fourth day .. | 6·5 | 2,200,000 | 408,000 | 97 | 2 | 1 | — | — | Present | None |
| W.R.[1] | M. | 51 | Acute myeloid leuchæmia. | Nine days before treatment .. | 3·4 | 1,500,000 | 48,600 | 5 | 29 | 55 | 8 | 3 | Present | Scanty |
| | | | | Seven days before treatment .. | 4·5 | — | 82,700 | 3 | 20 | 67 | 10 | — | Present | Scanty |
| | | | | Six days before treatment .. | 3·1 | — | 77,000 | 8 | 5 | 74 | 12 | 2 | Present | Scanty |
| | | | | Five days before treatment .. | 3·4 | — | 68,000 | 11 | 20 | 62 | 6 | 1 | 1 | Scanty |
| | | | | Two days before treatment .. | 3·1 | — | 83,000 | 14 | 21 | 57 | 7 | — | 1 | Scanty |
| | | | | First day .. | 3·5 | 1,150,000 | 148,000 | 13 | 23 | 55 | 9 | — | Present | Scanty |
| | | | | Second day .. | 2·8 | 1,100,000 | 181,000 | 19 | 22 | 55 | 4 | — | Present | Scanty |

[1] Patient died.

day onwards it was diluted with 100 cubic centimetres of 0·5% hydrochloric acid immediately before it was eaten, or 100 cubic centimetres of 0·5% hydrochloric acid were added to the minced placenta, which was left standing for about half an hour in the cold before the meal. A blood count before the first placental meal revealed that the red cells numbered 3,100,000 and the white cells 112,100 per cubic millimetre; the basal metabolic rate was +30%.

CASE II.—A male patient, aged forty-five years, had been suffering from chronic myeloid leuchæmia for twenty-six months. The last course of deep X-ray therapy was completed four months before the first placental meal. The patient had enlarged spleen and axillary glands. A blood count before the beginning of the experiment revealed that the red cells numbered 4,000,000 and the white cells 91,100 per cubic millimetre; the hæmoglobin value was 90% (Sahli).

In both cases pronounced diuresis occurred after the placental meals; otherwise no abnormality was detected. It was evident from the blood counts as well as from the size of the spleen and internal organs that there was no diminution in the leuchæmic state after one month's treatment, when the experiment was terminated.

### Comment.

Fresh placenta given by mouth does not influence the course of chronic myeloid leuchæmia.

### VITAMIN *C* IN LEUCHÆMIA.

Enfinger and Gaethgens reported a case of myeloid leuchæmia in which treatment with 200 milligrammes per day of vitamin *C* given intravenously for ten days produced great improvement. The patient was a female, aged fifty-five years, with a leucocyte count of 27,450 per cubic millimetre and a typical leuchæmic blood picture, the percentage of myelocytes being 21 and that of myeloblasts 8·0. According to their findings, the leucocytes decreased after four days of treatment to half their previous number, and decreased further to 3,500 per cubic millimetre after ten days of treatment. The hæmoglobin value and the number of erythrocytes doubled and the hæmorrhagic diathesis disappeared. After six weeks the leucocytes numbered 4,500 per cubic millimetre, only a few myelocytes being seen in the blood film.

In order to obtain more information about the action of vitamin *C* in leuchæmia, three patients suffering from chronic myeloid leuchæmia were given each day intravenous injections of 200 milligrammes of vitamin *C* (Cantan Bayer). The blood was examined periodically and a differential count was made. In the differentiation of cells, 200 cells were counted for every 10,000 leucocytes per cubic millimetre. It must be emphasized that the three leuchæmic patients treated have been known to suffer from leuchæmia and have been under clinical observation for a long period. All of them have had weekly blood examinations since the diagnosis of leuchæmia was made. The findings are shown in Table III.

None of the patients improved clinically during the ten days of treatment; there was no improvement of general health nor any decrease in the splenic tumour or in the enlarged liver and lymph nodules. It may be added that in the month following the injection of vitamin *C* the condition of all the patients became worse and they had to be treated with deep X rays and arsenic.

I therefore cannot confirm the results of Enfinger and Gaethgens, and believe that in their case the diagnosis of leuchæmia was doubtful.

### Comment.

The intravenous injection of 200 milligrammes of vitamin *C* per day over a period of ten days had no beneficial effect in three cases of chronic myeloid leuchæmia. Thus the findings of Enfinger and Gaethgens were not confirmed.

### MYELOID LEUCHÆMIA AND "PRONTOSIL" (BAYER).

Streptococci, staphylococci, pneumococci and many other infectious agents have been isolated in cases of leuchæmia and also have been suspected of being the cause of the disease (Forkner).

After so many good reports of treatment of infectious diseases with "Prontosil" it was decided to try the drug in cases of leuchæmia.

In order to study the action of "Prontosil" (Bayer) in cases of myeloid leuchæmia, three patients suffering from chronic myeloid leuchæmia and three patients suffering from acute myeloid leuchæmia were treated. The patients were kept in their beds in the clinic and their blood was examined daily. "Prontosil" was given for five days in doses of one gramme at intervals of four hours. The daily dose was six grammes. None of the patients showed any improvement during or after the administration of "Prontosil"; the number of white cells, the number of red cells and the enlarged lymph glands or spleen did not improve. Two patients with acute leuchæmia died during the treatment, one on the second day, the other on the fifth day.

### Comment.

"Prontosil" (Bayer) had no curative or beneficial effect in six cases of myeloid leuchæmia. This fact is not in favour of the hypothesis that leuchæmia is an infectious disease caused by streptococci, staphylococci, pneumococci or other infections.

### Bibliography.

C. E. Forkner: "Leukæmia and Allied Disorders", 1938.

H. Enfinger and G. Gaehtgens: *"Über die Wirkung des Vitamin C auf das pathologischen veranderte weisse Benthold"*, *Klinische Wochenschrift*, Volume CI, 1936, page 1836.

## Reviews.

### A YEAR BOOK OF MEDICINE.

LAST year Butterworth and Company issued the first annual supplement to the "British Encyclopædia of Medical Practice" in the form of a volume entitled "Surveys and Abstracts". The volume could be bought separately from the encyclopædia. The volume of "Surveys and Abstracts" for 1940 has been published[1] and is welcomed as a worthy successor to last year's production. The book is under the general editorship of Sir Humphry Rolleston, and as before is divided into three sections: I, "Critical Surveys"; II, "Drugs"; III, "Abstracts of Medical Literature". This arrangement has its advantages in that it allows the editor to include discussion on subjects which cannot be adequately dealt with by abstracts. Less space has been given to Part I this year than last—126 pages as against 162—but the range of subjects seems to be entirely adequate. We have chapters on general medicine, general surgery, obstetrics and gynæcology (the latter section full of good material), alimentary diseases, diseases of the blood-forming organs, blood transfusion, injuries to the ear, mental diseases, nervous diseases, tropical medicine, tick-bite fever, venereal diseases, tuberculosis, radiography and radiotherapy, recent work in anæsthetics, chemical pathology (an excellent contribution). It must be very difficult to write a chapter for a year book on recent developments in drug therapy, and there will always be those who would include something that has been omitted or omit something mentioned. We must therefore content ourselves with stating that after an introduction on the war and supplies of drugs Dr. W. J. Dilling includes sections on vitamins, sex hormones, sulphonamide compounds, drugs acting on the heart, sedatives and hypnotics, drugs for tropical diseases, heparin, tetanus toxoid. The section devoted to abstracts is comprehensive. Among the more important sections is one on injuries, including the treatment of wounds. Surgical diseases of the kidney come in for a good deal of notice, and recent work on calculi has been included. In the section on pharmacology many papers on sulphonamide compounds are mentioned. The abstracts on the vitamins are full of interest and give a really good idea of present-day knowledge—the abstracts have been skilfully prepared (as indeed they have throughout the work) and the result is a comprehensive article.

From the foregoing it will be clear to readers that the book has a wide scope; it is recommended with the utmost confidence. A word of congratulation is due to Dr. Adam Clark and Dr. G. Faulkner, the "publishing editor" and the sub-editor, whose work is obviously of a high order.

[1] "The British Encyclopædia of Medical Practice, including Medicine, Surgery, Obstetrics, Gynæcology and other Special Subjects, Surveys and Abstracts, 1940", under the general editorship of Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., D.Sc., D.C.L., LL.D.; Publishing Editor, A. Clark, L.M.S.S.A.; Sub-Editor, G. Faulkner, D.Sc.; 1941. London: Butterworth and Company (Publishers) Limited. Super royal 8vo, pp. 659, with illustrations. Price: 33s. 6d. net.

The Medical Journal of Australia

SATURDAY, NOVEMBER 22, 1941.

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## THE ASSOCIATION AND THE PUBLIC.

THAT it should be necessary in this so-called enlightened age and in so progressive and well informed a country as Australia to publish in this journal any statement on the aims and objects of the British Medical Association, will at first sight seem absurd. But knowledge is not so widespread as is sometimes thought and memories are short; many people, also, go through the world wearing blinkers—they see only what they want to see and even then lose all perspective. Others do not want to see or to believe anything outside their own imaginings. When we have to do with ignorance, forgetfulness, restricted vision and prejudice we are in difficulties. Members of the British Medical Association in Australia have to face the unpleasant fact that, though as individual medical attendants of individual members of the community they are held in high esteem by their patients and may give advice knowing that it will be followed to the letter, as members of "the B.M.A." they are supposed to be guilty of unreasoning and unreasonable adherence to a code that seeks its own advantage at the expense of others, of dragooning members of the profession who do not belong to the Association, and of many ill-defined acts of impropriety. This distrust of the Association and its activities may be counteracted in two ways. The first is by a declaration at suitable times and seasons of the aims and objects of the Association, what its members set themselves to do and what they accomplish, and also of its powers. The second is by the constant demonstration that the objects of the Association can be and are the mainsprings of action in the scientific and corporate, in the entire, lives of its members. The first is the province of publications such as THE MEDICAL JOURNAL OF AUSTRALIA and of Branch councils, Branch officers and such members as have the ear of the public. The second is in the hands of the members themselves, backed perhaps by the moral support of Branch organization. For the vindication of the Association both are necessary, and of the two the second is the more important. Beliefs put into practice may alone carry conviction, but words without works are dead.

The British Medical Association had its beginnings in 1832 when Charles Hastings, a general practitioner of Worcester, England, founded the Provincial Medical and Surgical Association. Out of the smallest beginnings the society grew and spread until it lost its early provincialism and became the leading medical society in the United Kingdom. The name was changed and the body became known as the British Medical Association. The first fact that must be stated with clear emphasis is that the British Medical Association is a voluntary association of members who band themselves together to achieve certain objects. It is in no sense a statutory body. This means that it has in law no power over the right of medical graduates to engage in practice. The British Medical Association, which has its headquarters in London, has spread its wings till they cover the whole of the Empire, and Australia is only one of the spheres outside the United Kingdom where its beneficent influence has been shed. The Australian Branches have the standing of what are known in the United Kingdom as Divisions, and they carry on their functions under the ægis of the Federal Council. Their objects of existence are the same as those of the Parent Body—the promotion of the medical and allied sciences and the maintenance of the honour and interests of the medical profession. At the risk of being considered tedious, we must again insist that the British Medical Association's objects have nothing to do with the rights of a medical graduate to practise his or her profession. In Great Britain power to register men and women as qualified to practise medicine, and power to remove their names from the register, is vested in the General Medical Council, a legally constituted body. In Australia these duties are entrusted in the several States to the medical boards, and these are legally constituted bodies with certain executive powers. But this is a digression, and we must return to the objects of the British Medical Association. The general public does not realize what an exacting life that of a medical practitioner is in regard to the study that must be constantly pursued. To further this study is the main activity of the Association. Each of the Australian Branches holds at least one meeting a month for the study of disease, either by the reading and discussion of papers or by clinical demonstration and discussion. Most of these meetings are reported in this journal so that those who are not able to attend meetings shall not be at a loss. The public knows little about these meetings and the problems discussed at them, and there is no reason why it should. Obviously, however, the public benefits from them, for the more completely medical practitioners have studied disease, the more efficient will be the service given to the public. When we say that the British Medical Association has to maintain the honour of the medical profession, we refer to the ethical standard that must be observed by all its members. The general public often confuses ethics, which is a question of morals, with etiquette, which has to do with manners. It is clear here also that the maintenance of a high ethical or moral standard in medicine is an advantage to the general public. When the medical practice of a country is on a high ethical plane, it is free from debasing usages which seize on illness as opportunism and make the purse more important than the patient. The Branches of the British Medical Association can and do discipline their members when occasion arises, but these occasions are not legal

procedures and are not known to the public, nor for that matter to those Branch members outside the official circles appointed to deal with such questions. The last and, we submit, the least important of the Association's activities is that which is concerned with the interests of the profession. This covers a wide sphere and it is possibly in connexion with matters coming under this heading that the public receives a false impression of what the Association tries to do. As society is constituted and as medicine is at present practised, fees have to be charged for attendance on persons who are ill. The "interests" of the profession include many matters and the question of payment for services rendered is one of them. The Australian Branches of the British Medical Association do not control the fees of private practice, but in regard to contract practice they hold a watching brief for members and have contrived to establish agreements which generally speaking are acceptable to the profession and certainly provide a satisfactory service to the persons concerned. Another sphere in which the "interests" of the profession are dealt with by some, if not all, of the Australian Branches, is that of hospital practice. Here, as in other matters, the result is, we hold, equally to the advantage of the patient and the attending doctor. This does not imply that the Branch councils regard hospital practice in Australia as having reached the highest peak of efficiency and as not capable of improvement. To hold such a view would be foolish, for our present state of civilization is not perfect and there must be advance in every side of social life. Of the powers of the Association it is not necessary to write a great deal. As a voluntary and private association of members it requires members to obey its rules, rules to which they assent by the act of becoming members. It can therefore control its own members, but it has no control of any kind over medical practitioners who have not become members. This cannot be emphasized too much or too often; nor can the fact that there is no rule or regulation that prevents members of the Association from consulting with non-members. Though by far the greater number of reputable members of the medical profession in Australia have joined the British Medical Association, there are some who have not sought admission to its ranks.

So much for a declaration of the aims and objects of the British Medical Association and of its powers. Of the attitude of members to the Association and of their adherence to its standards of life and conduct we do not propose to write at present; we hope that this side of the question will not be forgotten by members when they are thinking of the relationship of their association with the public.

Readers of this journal will agree that a discussion on the relationship of the British Medical Association to the public is not a novelty to this journal or to any other journal serving members of the Association. From time to time a discussion of this kind becomes necessary. On this occasion we have been compelled to draw attention to the subject by reason of certain remarks made in the Legislative Assembly of New South Wales in August of this year by the Honourable Maurice O'Sullivan, Minister of Transport, and by the Premier, the Honourable William John McKell. The occurrence is reported in *Hansard* of August 26, 1941, on page 610, under the heading "Questions without Notice". Mr. G. C. Gollan, member for Parramatta, asked the following question:

Can the Minister for Transport say whether it is a fact that notices have been placed in Eveleigh and other workshops notifying men who are not associated with a union that they must become registered by a certain date? If in this liberty-loving land of Australia such a thing is a fact, will the Minister indicate what method he will adopt to coerce these men to join a union?

The Honourable Maurice O'Sullivan replied in the following terms:

I believe it is a fact that notices have been placed in the workshops intimating that employees must become members of unions recognized by the State or Federal Arbitration Court. What we would do to them should they refuse to join is a matter that may never have to be considered, but I should like to point out to the hon. member that unless a doctor belongs to the B.M.A. in this State he cannot practise as a doctor, and that if any man joins a friendly society, irrespective of what section it represents, the privileges and benefits cease if he does not pay his subscription. If the railway men do not pay we will find some way of asking them to pay.

This reply was followed by a question from Mr. R. S. Vincent, member for Raleigh, who said:

Will the Minister indicate the source from which the B.M.A. derives its authority, if any, to prevent medical men from practising their profession, and if the B.M.A. does possess such a power will he see to it that the power is eliminated?

To this question Mr. G. C. Gollan added another:

Is it not a fact that there are doctors practising in New South Wales who do not belong to the British Medical Association?

To these questions the Premier, the Honourable William John McKell, replied as follows:

Every hon. member knows perfectly well that a doctor who is not a member of the British Medical Association is not recognized, and that members of that association will not consult with him or work with him. Hon. members know perfectly well that the threat of ostracism by the British Medical Association makes it for all practical purposes impossible for a man to practise in the medical profession outside of that association.

That responsible ministers of His Majesty's Government should make such statements as these is much to be regretted. These are days when the medical profession of Australia, with all other Australians, is working for and hoping to achieve union and not dissension. The making of incorrect statements which, because of their incorrectness, are likely to be both disheartening and damaging to a large section of the community, is, to say the least of it, not helpful. We refrain from further comment in the hope that the good sense of the Minister and of the Premier, Mr. McKell, will prevent a repetition of such a regrettable incident.

## Current Comment.

### BLOOD STUDIES IN PARATHYREOID TETANY.

POST-OPERATIVE parathyreoid tetany is not very common today, but it may be unavoidable, and a few sufferers are seen each year, even at "thyreoid clinics". The study of this troublesome sequela has added important facts to our knowledge of parathyreoid function. In fact, nearly all the greatest advances in endocrinology are due to study of the results of removal or destruction of one or another of

the ductless glands. J. Douglas Robertson has recently had the opportunity of studying seven patients suffering from parathyreoid tetany which began a few days after subtotal thyreoidectomy for hyperthyreoidism.[1] He investigated the calcium and phosphorus balance of all except one patient before treatment to control the tetany was begun. For controls he investigated normal subjects and those in whom subtotal thyreoidectomy had been an unqualified success. He found a diminished calcium loss in tetany as compared with normal subjects and in thyreotoxic patients after thyreoidectomy. The mean negative balance for the seven individuals was −0·23 gramme per three-day period. The mean phosphorus loss, under the same conditions, was −1·02 grammes as compared with a normal loss of −10·54 grammes, and after uncomplicated subtotal thyreoidectomy of −2·41 grammes. The latter figure does not represent a significant difference between the loss in parathyreoid tetany and in the period following a successful subtotal thyreoidectomy. Further study of the mode of loss of calcium of a patient with severe tetany revealed that there was a diminution in the excretion of calcium in both urine and fæces, and that as the serum calcium level fell so the level of inorganic phosphorus in the serum rose.

Albright and Ellsworth have pointed out that a serum calcium level of 8·5 milligrammes *per centum* appears to be the level of renal threshold for calcium, but in one of Robertson's patients 23% of the total calcium excretion was passed in the urine at a serum calcium level of 5·5 milligrammes *per centum*. (Thus in seven cases of tetany there was found to be a diminished calcium loss, which is in agreement with the previous work.) If there is a threshold value for normal people of 8·5 milligrammes *per centum*, it is surprising that the accepted value for normal blood calcium, about 10 milligrammes *per centum*, should exceed it. Experiments upon the excretion of calcium injected into the veins should be able to determine this point.

Phosphorus excretion is also diminished after parathyreoidectomy, and this is clearly shown by Robertson's figures. Of the seven patients, three had a positive phosphorus balance on an average intake of almost 0·39 gramme of phosphorus daily. There is, however, no significant difference between this loss and that occurring after subtotal thyreoidectomy without parathyreoid tetany. As much as 56% of the phosphorus was excreted in the fæces. The low partition of the phosphorus in the urine as compared with the fæces, which has been considered a feature of parathyreoid tetany, is also found after subtotal thyreoidectomy. In idiopathic hypoparathyreoidism a normal urinary excretion of phosphorus is found. The work further confirms the fact that a considerable increase in the inorganic phosphorus content of the serum takes place at low levels of serum calcium.

Aub and his colleagues think that the parathyreoid hormone keeps the serum calcium above threshold level. This investigation contains a report of one case in seven in which this view of the effect of parathyreoid hormone is not supported. It is not enough evidence to call for the abandonment of Aub's hypothesis, particularly as tetany following subtotal thyreoidectomy does not prove complete ablation of all parathyreoid tissue.

## ACUTE HÆMOLYTIC ANÆMIA FROM THE SULPHONAMIDES.

WHEREAS attention has frequently been drawn to leucopenia and agranulocytosis as complications of sulphonamide therapy, very little stress has been placed on the association of acute hæmolytic anæmia with sulphonamide therapy. Most physicians now realize the advisability of having leucocyte and differential blood counts made during the administration of the sulphonamides, but usually possible changes in the red blood cells are overlooked. The rarity of acute hæmolytic anæmia as a complication of sulphonamide therapy at first naturally led to the suggestion that the association was coincidental, but that this is unlikely is shown by the apparent specific effect of the sulphonamides in some instances and by the increasing number of cases of acute hæmolytic anæmia which have been reported as related to sulphonamide administration. C. L. Fox and R. Ottenberg[1] have added another nine cases of acute hæmolytic anæmia in the course of sulphanilamide or sulphapyridine therapy, with six deaths. The number of such cases of acute hæmolytic anæmia reported still does not total a score, and although T. E. Machella and G. M. Higgins[2] have shown that in rats it was possible to produce an anæmia the degree of which was dependent on the dose of the sulphanilamide and on the duration of the administration and from which recovery could occur on cessation of the drug, it must be admitted that there exists a close resemblance between these cases associated with the administration of the sulphonamides and idiopathic cases of acute hæmolytic anæmia. The four patients whose history Fox and Ottenberg describe in detail received no more sulphonamide than has been given to many patients without untoward effects—the largest dose was 48 grammes over a period of four days. Although this is a relatively large course, it is usually well tolerated by most adults. Most patients receiving large doses of the sulphonamides over long periods of time produce correspondingly large amounts of methæmoglobin in the red cells, but in those patients in whom acute hæmolytic anæmia develops it appears early and after only moderate doses of the drugs. From a study of the hæmoglobin derivatives in the serum, red cells and urine in their cases, these authors suggest that certain individuals form unusual oxidation products which are hæmolytic and which are present in or affect chiefly the red cells containing methæmoglobin. As Fox and Ottenberg point out, none of the other drugs known to cause drug allergy produce hæmolytic anæmia, and, furthermore, drug fever and skin rashes, complications of sulphonamide therapy more readily attributable to drug allergy, are not associated with hæmolytic anæmia. Further study of the problem is obviously necessary before it can be clarified.

[1] *The Lancet*, August 9, 1941.

## THE END-RESULTS OF CORONARY THROMBOSIS.

IN December of last year a leading article in this journal was devoted to the ultimate prognosis and rehabilitation in coronary occlusion. Discussion centred round an article by A. M. Master and Simon Dack, who stated in their general conclusions that an attack of coronary thrombosis was not in itself sufficient reason for permanent disability. The patients reviewed by these observers numbered 415 and the whole discussion went to show that a patient recovering from an attack of coronary thrombosis had much more hope than he used to have. A recent study confirming this view comes from E. F. Bland and P. D. White, of the Massachusetts General Hospital,[3] who have reviewed the condition of 200 patients with coronary thrombosis and myocardial infarction seen by them in the decade 1920 to 1930. Of the entire series, 38 died within the first four weeks of their original attack. Of the remaining 162 patients, almost one-third (31%) survived the ten-year period, and it is calculated that another decade or longer will be required to complete the after-history of this group. Of the 162 patients, 34% were able to carry on without cardiac symptoms, 39% had to limit their effort because of *angina pectoris*, and 27% had dyspnœa on effort which was the chief cause for limitation of effort. Bland and White conclude with the cheering statement that as more mild cases of coronary thrombosis with myocardial infarction are now being recognized, even more favourable reports may be expected in the future.

[1] *The Journal of Clinical Investigation*, September, 1941.
[2] *The American Journal of the Medical Sciences*, December, 1939.
[3] *The Journal of the American Medical Association*, October 4, 1941.

# Abstracts from Medical Literature.

## PÆDIATRICS.

### A Hospital Study of Poliomyelitis.

LEO LITTER (*Archives of Pediatrics*, July, 1941) draws attention to the fact that acute anterior poliomyelitis, with its protean manifestations, is a conspicuous example of a communicable disease in which the diagnosis is overlooked or which is simulated by other diseases. The difficulty in the differentiation of poliomyelitis from general systemic or central nervous system diseases is great, because the former is often present in the preparalytic or abortive stage. Twenty years ago the diagnosis of this disease was made only after the paralysis had occurred. Today the diagnosis can be made in the preparalytic stage. During the summer of 1939, 65 patients were admitted to the Kingston Avenue Hospital on the poliomyelitis service. The diagnosis was suspected in only 29 cases and overlooked in the remaining 36. Of patients in the latter group, 21 entered the hospital with various diagnoses, but were subsequently proven to be suffering from poliomyelitis. The remaining 15 turned out to be suffering from something else. In all, 50 patients suffering from poliomyelitis were treated, ranging in age from sixteen months to thirty years. The cases were divided into bulbar, ascending, encephalitic, paralytic and non-paralytic types. Five deaths occurred, all within the first week. The Schick test gave a positive reaction in half of the cases. The author points out that poliomyelitis is not so prevalent in regions where the children have been inoculated against diphtheria, and that other observations indicate a relationship between susceptibility to diphtheria and poliomyelitis. The usual order of symptoms—fever, vomiting and headache—prevailed in the majority of patients admitted to hospital. Absence of the knee jerks was the most prevalent sign. Superficial and deep reflexes were next in order. Rigidity and stiffness of the neck were present in many cases. In regard to paralysis, one or both legs were the parts most frequently involved. The spinal musculature was involved in 16 and the diaphragm and intercostals in six cases. The cranial nerves involved were facial, glosso-pharyngeal and hypoglossal. The frequency of abdominal pain was relatively high, and because of its severity a number of these patients were considered to be suffering from an acute surgical abdominal condition prior to admission to hospital. Lumbar puncture was performed in all but one case. Examination of the spinal fluid revealed it to be cloudy in three cases, clear and under increased pressure in most of the others. The lowest cell count was 0 and the highest 650 cells per cubic millimetre, the average cell count being 98. In several cases less than 10 cells were found. The predominating type of cell was the lymphocyte. High counts did not necessarily mean a severe illness. The lowest counts were found in the bulbar types and the highest counts in the spinal poliomyelitis types. Total protein varied between 28 and 265 milligrammes per 100 cubic centimetres. Sugar was present in normal amounts in 24 instances, and slightly increased in the others. Chlorides were present within normal limits in all cases. The amount of globulin increase did not bear any definite relationship to the number of cells in the spinal fluid. The author discusses in detail the differential diagnosis and orthopædic treatment, and gives a survey of a follow-up study of all except four of the series.

### Congestive Failure in Children Suffering from Active Rheumatic Fever.

BERNARD J. WALSH AND HOWARD B. SPRAGUE (*American Journal of Diseases of Children*, May, 1941) point out that although it is now commonly recognized that congestive failure in children with rheumatic heart disease is due to the presence of active rheumatic fever, the clinical features of heart failure in such patients are less well known. The authors describe these features from observations based on a study of 44 children between the ages of three and fifteen years. The initial signs of cardiac failure in these children are enlargement of the liver, puffiness of the face, and unexpected gain in weight. In addition to these signs which have been described by other observers, the authors have noted three others signs which have not heretofore been adequately emphasized: (i) the shift of the electrical axis to the right in the presence of prolonged heart failure, (ii) the development of a diastolic gallop localized in the second and third interspaces at the left sternal border, and (iii) an early rise of venous pressure above normal. Increase in the size of the liver is an early sign of heart failure in children. In the experience of the authors it has been the initial clinical sign in each case, appearing in many instances a week or more before other clinical evidence of heart failure. Similarly, when improvement has occurred, the liver has remained palpable some time after the peripheral œdema has disappeared. Puffiness of the face is frequently the first apparent change marking the development of heart failure in children sick with rheumatic fever. In a few children the puffiness was considerable, causing them to resemble patients with nephrosis. An unexpected gain in weight was invariably associated with the facial œdema, both being due to fluid retention. There was a tendency to right axis deviation of the electrocardiogram in the presence of continuing heart failure, even in patients with established aortic regurgitation. If recovery occurred, the electrical axis gradually returned to normal with the improvement and recovery of the patient. A few children with heart failure, probably not more than one in five, have shown a well-marked diastolic gallop, best heard in the second and third interspaces at the left sternal border. The authors regard this as an additional important point of evidence in support of their belief that insufficiency of the right ventricle is the underlying physiological cause of the early rise in venous pressure, enlargement of the liver, peripheral œdema, freedom from râles and absence of orthopnœa in some patients. An elevated venous pressure was found to be an invariable accompaniment of the previously mentioned signs. The venous pressure was found to rise above normal concomitantly with enlargement of the liver when heart failure developed in a child with rheumatic fever. Obvious engorgement of the veins of the neck, however, was strikingly absent in spite of abnormally high venous pressure. After diuresis and subsidence of œdema subsequent to the use of a diuretic or digitalis the venous pressure promptly decreased and in those cases in which all evidence of congestive failure disappeared it returned to within its normal limits (50 to 150 millimetres of physiological sodium chloride solution).

### Blood Changes Produced by Dehydration in Infancy.

A. G. V. ALDRIDGE (*Archives of Disease in Childhood*, June, 1941) has studied the blood changes in a series of fifty-one infants showing varying degrees of dehydration (35 suffering from gastro-enteritis and 16 from pyloric stenosis). The red blood cell count was raised, the average count being well over 5,000,000 per cubic millimetre. This represents a considerable increase in the red count in infants of this age, although some of the increase may be due to nutritional anæmia. The hæmoglobin is also increased, but often to a less degree than the red cell count because of the presence of hypochromic anæmia. Estimation of the hæmoglobin alone was not an adequate indication of hæmoconcentration. When allowance was made for age and any nutritional anæmia that might have been present, the hæmatocrit reading was considerably above normal. The plasma chloride in gastro-enteritis was variable; the average for the series was raised (651 milligrammes *per centum*), but in some cases the values were below normal. The level of the plasma chloride did not necessarily vary with the degree of dehydration or clinical condition. It was shown that an apparent, if not actual, rise in concentration of plasma chloride in gastro-enteritis and dehydration was due to: (*a*) the relatively small amount of chloride as compared with base lost; (*b*) the concentration of the circulating blood; and (*c*) renal insufficiency. In pyloric stenosis the plasma chloride content was either diminished slightly or on the low side of normal. The level of plasma protein in gastro-enteritis was on the average a little higher than in a series of normal infants. The plasma protein concentration cannot be used as an indication of the state of hydration of the circulating blood. The plasma protein content in pyloric stenosis was slightly above normal. In this series of cases no definite relation was found between concentration of plasma protein and blood cell, hæmoglobin and hæmatocrit reading, except that all values tend to be raised above normal in dehydration.

### Rheumatic Fever in a Newborn Infant.

EDWARD J. DERRENHOLZ AND ALWIN C. RAMBAR (*American Journal of Diseases of Children*, May, 1941) record particulars of a probable cause of rheumatic fever in an infant eighteen days old. When the infant was seven days old the mother suddenly showed painful, swollen, tender joints (right elbow and ankles) and fever accompanied by profuse sweats. The symptoms promptly subsided to large doses of salicylates. Three days after the onset of the mother's symptoms the baby had a slight fever and cried when her right arm was touched. She became irritable, took her feedings poorly, vomited two or three times daily, had profuse sweats

and cried when she was picked up or when the bed clothes were disturbed. The temperature varied from 100° to 103° F. After a few days swelling became evident over both ankles, which were tender and slightly reddened. The swelling then subsided, after which the right wrist became reddened and swollen. The infant was given acetylsalicylic acid and sodium bicarbonate and was discharged from hospital after two weeks, apparently entirely recovered. The diagnosis pointed to rheumatic arthritis despite the great rarity of that disease at this age. Considered, however, as possible diagnoses were congenital syphilis, gonorrhœal arthritis and sepsis, and as less likely, tuberculosis, tetany and scurvy. Syphilis was ruled out by the failure of the mother to react to the Wassermann test and by the normal skiagrams of the infant's long bones. When the Wassermann test was applied to the infant's blood at the age of three months no reaction occurred. Gonorrhœal arthritis was excluded by the absence of a focus, such as conjunctivitis or vaginitis, and by the mother's normal vaginal smears and failure to react to complement fixation tests for gonorrhœa. Sepsis was ruled out by failure to culture organisms in the blood of both mother and baby, by the absence of primary or metastatic foci in both mother and child, and by the rapid recovery following the administration of salicylates. Scurvy in the newborn is extremely rare, if it occurs at all. The diagnosis was eliminated, however, by the normal level of ascorbic acid in the blood and by the absence of a history of vitamin *C* deficiency in the mother. Tuberculosis of the bones was not seriously considered and was ruled out by normal skiagrams, the time of onset, the failure to react to the tuberculin test and the rapid subsidence of symptoms. Tetany of the newborn was unlikely in view of the normal blood chemistry and the absence of neuromuscular hyperirritability.

## ORTHOPÆDIC SURGERY.

### Fractures and Dislocations of the Cervical Portion of the Spine.

WILLIAM ARTHUR CLARK (*Archives of Surgery*, March, 1941) reviews 81 cases of fracture and dislocations of the cervical portion of the spine. Many types of trauma were responsible, more than half resulting from motor car accidents. Falls were responsible for 23·8%. The author states that dislocation alone may occur from slight trauma or without any trauma. Inflammatory weakening of the muscles and ligaments of the cervical region, notably of the first and second vertebræ, and congenital anomalies of the vertebræ may constitute a predilection to dislocation. Sneezing, coughing or sudden twisting of the head may be classed as muscular violence. In fractures or dislocations pain is not a prominent symptom, but tenderness on movement of the head is pronounced. A hyperflexed neck with the chin on the chest suggests bilateral dislocation. If the head is tilted to one side and rotated to the opposite side, there is usually unilateral dislocation. Unless extreme compression of two or more vertebral bodies is present, visible deformity is not likely to occur. Neural symptoms vary from slight tingling of the fingers to complete motor and sensory paralysis from the shoulders down. Fever, respiratory difficulty and priapism may all be present with high lesions accompanied by damage to the cord. In the writer's series symptoms of compression of the cord were present in 26·1% of cases; dislocation alone produced the paralyses in eight instances, fracture alone in three, and fracture dislocation in ten. Paralysis in all four limbs was present in thirteen cases; in five cases the legs only, and in one the arms alone were paralysed. Practically all cases of paralysis occurred in lesions of the fourth, fifth and sixth vertebræ. The absence of motor and sensory impairment with lesions above this level is explained by the fact that the bony canal of the second and third vertebræ is larger in proportion to the size of the cord. Loss of sensation was noted in 21·5% of cases. In all dislocations except one the superior vertebra was anterior to the one below. The sixth cervical vertebra was involved in more cases than any other, and in 49·4% of cases the lesion was in either the fifth or the sixth vertebra. This disagrees with the statement in some text-books that the third vertebra is the weakest part of the cervical portion of the spine. There were six cases of dislocation and five of fracture dislocation of the atlas, but no isolated fracture of this bone. No compression fracture of a vertebral body above the fifth was found. In fractures of all cervical vertebræ the body was fractured in 51·5% of cases. The treatment applied in 37·5% of cases was extension of the head followed by the use of an ambulatory cast or a brace. Manipulation followed by a cast was adopted in 6·8%, and in 15·9% a cast only was applied. Skeletal traction was applied in 5·7%. In 17% of the remainder little could be done for the local lesion because of the serious condition of the patient, and the treatment of a further 17% was not recorded. The writer recommends early attempts to reduce dislocations by manipulation in cases of severe or complete paralysis. The neck should be held in extension from the time of the accident, an emergency temporary halter being improvised. The Walton manipulation was used more frequently than the more forcible extension method of Taylor. Manipulation was successful in 55·5% of the cases in which it was tried. In 22·2% the position was improved, and in 22·2% manipulation failed to reduce the dislocation. Recurrence after good reduction occurred in 3·3% of cases. No open reductions, fusions or laminectomies were done in this series. The general mortality was 25·8%. Most of the deaths, 73·9%, occurred in the first five days and 39·1% succumbed in the first twenty-four hours.

### Calcium Deposits in the Shoulder and Subacromial Bursitis.

B. M. BOSWORTH (*The Journal of the American Medical Association*, May 31, 1941) discusses a survey of 12,122 shoulders examined for the presence of calcium deposits round the shoulder. The subjects examined were 5,061 presumably normal employees of an insurance company. They included 3,883 females and 1,178 males. Approximately 89% were under the age of forty years and 93% were employed in clerical work. In this group, in the course of routine annual fluoroscopic examination, visible calcium deposits were found in one or both shoulders of 2·7%. Deposits were found with greater relative frequency in males. The writer stresses the importance of fluoroscopy, by which means the shoulder can be examined in profile. In radiological examination calcium deposits may be missed. Consideration of age showed that the incidence of calcium deposits rose with the advance of years up to the age of fifty, after which it declined sharply. There was no indication that infection played any part in the process. Blood calcium readings were normal in all cases in which deposits were present. Occupation appears to play a part and the figures presented in table form show that women typists had a significantly higher incidence of deposits than women clerks. Consideration must be given to occupation as a causative factor, when the work involves constant abduction of the arms for months or years. In only seven of forty-one cases was a clear history of trauma given. Trauma appears to be incidental or at most the straw which broke the camel's back by precipitating an inevitable bursitis. Among those patients with unilateral deposits, the right shoulder was involved twice as often as the left. Of the involved shoulders, 51·5% had calcium in the supraspinatus, 44·5% had calcium in the infraspinatus and 23·3% had it in the *teres minor*. Calcium appeared subsequent to a fluoroscopic examination that failed to reveal an abnormality, three cases being discovered within as short a period as two months. Seventy of the 202 involved shoulders caused some degree of pain or discomfort. This varied from an occasional "twinge" to complete disability. Nocturnal discomfort was most frequently mentioned. The question of what form of treatment offers the best prospects of relief or cure is a difficult one. Some patients in the series had complete spontaneous remission of symptoms without treatment. The condition of others responded to heat therapy. Excision or irrigation of deposits was also practised. The author believes that prompt excision of the deposit is the best treatment for the acute attack.

### Repair of Old Rupture of Tendo Achillis.

ISADORE ZADEK (*The Journal of Bone and Joint Surgery*, October, 1940) reports a case of complete rupture of the *tendo Achillis* in a man, thirty-seven years of age. Seen one month after an accident, the upper ruptured end was conical in shape and the lower end bulbous and redundant. When the ends were trimmed, a gap of three inches separated them, with the upper portion of the defect at the musculotendinous junction. Three strips of *fascia lata*, six inches long and a half-inch wide, were then woven into splits made in the two portions of the cut tendon and sutured under slight tension with heavy chromicized gut. A plaster of Paris cast was applied from the toes to the knee with the foot in slight equinus. After eleven days a new walking cast was applied with the foot at a right angle. Several days later weight bearing, aided by crutches, was permitted. At the end of five weeks the patient was fitted with an ankle brace with attached footpiece to limit movement, and this was worn for five months. When last seen, two years after operation, the patient had full function in the limb and was carrying out his work of physical training instructor.

# Special Article.

## PUBLIC RELATIONS OF MEDICAL PRACTICE: HISTORY OF EVENTS IN NEW ZEALAND, NOVEMBER, 1941.

BY OUR SPECIAL CORRESPONDENT.

THE date of November 1 is a suitable one on which to describe the events, for today the universal general practitioner service was inaugurated—only one, but the greatest single, "benefit" offered by the *Social Security Act* of 1938. Not that there will be no more to say, even on the general practitioner service, in the future.

### In the Beginning.

In 1935, in the declining months of office of the National Party's Government, a departmental committee tabled a report in the House of Representatives on the subject of national health plans. There had also been earlier discussions, in 1929 and 1934, by the Hospital Boards' Association, but nothing in particular emerged.

Also in 1935, at the annual British Medical Association[1] conference in Dunedin in February, a special "National Health Insurance Committee" was appointed to investigate the subject. This committee persists to this day and has undertaken many important tasks.

In November, 1935, after an election in which all three parties featured national health insurance proposals, the Labour Party was returned for the first time. It commanded a large majority in the House. Early in February, 1936, the British Medical Association waited on the new Minister of Health, the Honourable P. Fraser (now Prime Minister), offering cooperation and asking for his confidence in relation to any future proposals. This was promised, but the British Medical Association claims that he was unable to fulfil his promise, and that at all subsequent stages the Government concealed its intentions and kept the Association in the dark until the last minute.

In 1936 the Government set up an investigation committee with the declared purpose of introducing a system of health insurance. This committee consisted wholly of Members of Parliament of the Government party, and though it took evidence from interested parties, including the British Medical Association, there is reason to doubt whether such evidence made much impression on the preconceived ideas of the members of the committee. The only medical member of this committee was a junior practitioner who had been elected Member of Parliament for one of the southern seats.

The substance of the British Medical Association's representation to this committee in February, 1937, included a complete medical service for the indigent, and a contributory system of insurance for all others who were unable to provide themselves with hospital treatment, and laboratory and specialist services. The family doctors' services should be provided for by the people themselves, either privately or or through friendly societies. Reform of the hospital system and more attention to preventive medicine and research were also recommended.

The Parliamentary Committee expressed itself as disappointed with the views of the British Medical Association, and later its chairman hinted that its thoughts were running along the lines of a universal free medical service for everyone, based on a general practitioner service, but later to include hospitals, laboratory, specialists *et cetera*. He asked the British Medical Association to amplify its previous suggestions by preparing a plan capable of being introduced in sections, incomplete at first, but finally to be comprehensive. He also toured the country and explained his ideas to the medical men—not committing the Government. The basis of his proposals was a capitation system at one pound per head of population *plus* mileage and other extras, applicable to everyone in the community. He indicated that the doctors might expect to receive as much as they had done in the past.

In July, 1937, the British Medical Association presented its plan to the Minister and to the committee. This provided a sectional approach to a complete service, though not along the lines of the Government's universal service. It followed in general the lines referred to above, and was adopted after discussion by all divisions of the British Medical Association.

[1] The words British Medical Association are used throughout this article to indicate the New Zealand Branch of the British Medical Association.

Later in 1937 Sir Henry Brackenbury, a well-known advocate of national health insurance, visited New Zealand by arrangement, and his advice and services were made available to the Government as well as the British Medical Association. He agreed with the British Medical Association that the universal free service would yield poor service and introduce unnecessary and undesirable control of public and the profession. He rendered a report to the Government in terms almost identical with the British Medical Association's report. He thought a universal general practitioner service of a quality similar to what currently obtained could not be given under £1 11s. 6d. per head, excluding the other services planned.

The Government committee next reported to the Minister, but the contents of this report were not made known to the British Medical Association, though this was requested.

From December, 1937, to March, 1938, meetings and correspondence took place between ministers, departmental officers and British Medical Association representatives. Further points were elaborated by the British Medical Association, but no common ground could be reached, particularly with Mr. Nash (Finance Minister). Mr. Fraser seemed more ready to appreciate the arguments of the British Medical Association. The British Medical Association complained that the ministers' approach and motive was a political one, and that Mr. Nash at least had not troubled to study its memoranda. Evasive answers were given to the request for the Government's proposals for consideration.

In April, 1938, a parliamentary select committee was set up to take evidence and prepare the ground for the Social Security Bill to be introduced later in the year. The British Medical Association again represented its views, but complained that, like those of an experienced actuary lent by the British Government, they were brushed aside, and that in no way could the committee's deliberations be regarded as a dispassionate inquiry into a technical subject along non-political lines. Later, when the committee had presented its report, the British Medical Association's request for a copy of it for discussion was refused.

In September, 1938, the Social Security Bill was presented to the House, and only after this was it submitted to the British Medical Association. Negotiations between ministers and the British Medical Association broke down. The bill was passed and became law shortly after.

### The Social Security Act, 1938.

The *Social Security Act*, 1938, had two main objects. It was intended to substitute for the existing system of non-contributory civil pensions a system of monetary benefits on a contributory basis. It also made provision for the inauguration of a system of medical, hospital and related benefits. The money was to come from a new social security tax of one shilling in the pound, payable by practically everyone in the community, and replacing the old unemployment levy of eightpence in the pound, payable by a more limited clientele. The social security tax came into force on April 1, 1939, and has been regularly collected since.

The medical benefits were to consist of a general practitioner service available to every person in the community. Maternity benefits available on a similar basis were limited to such service as a general practitioner ordinarily gave. Pharmaceutical benefits were to include all ordinary prescriptions and appliances. Hospital benefits were to consist of the payment to the hospital (whether public or private) of a portion of the fees charged to the patient, thus relieving the patient in part, and ensuring to the public hospital authorities payment where sometimes—as with the indigent and the elusive—there had been none.

Apart from these four benefits, the bill foreshadowed, but did not provide for, a number of others—for example, radiological, laboratory, anæsthetic, specialist, and consultant, dental, ambulance, home nursing and domestic assistance benefits.

### General Election: Negotiations Resumed.

With the passage of the bill and the approach of a general election things became very heated. The British Medical Association called upon its members to resist the bill, to vest their rights to accept or refuse contracts under it in the local committee, and to give donations to a fighting fund. Members, including high officials of the British Medical Association, were prominent in the election campaign, mostly for the National Party, and the Social Security Bill was freely used in endeavours to discredit the Labour Party.

The election (November, 1938) was a hotly contested one, in which the Social Security Bill was the dominant issue. The Labour Party was returned to power with an absolute majority.

In January, 1939, the Minister of Health (Mr. Fraser) approached the British Medical Association with a view to resuming negotiations. The bill had been promised to come into force on April 1, 1939. It was suggested that common ground might be found in a system of "payment per service rendered" in lieu of a capitation system. It was known that some general practitioners were in favour of the former, particularly if the patient were made responsible on each occasion for a part of the fee—say two shillings and sixpence of a half-guinea fee—as a bar to frivolous calls. It was known, however, that the Government would not consider any scheme which interposed payment between patient and doctor.

In March the Minister circulated documents to medical practitioners describing the bill and its benefits. The rate of remuneration for general practitioner service was not specified, nor its manner of distribution. It was simply to come from a central practitioners' fund, which was to be formed either on a capitation basis or on an estimated-amount-of-service basis. Later mention of medical benefits was dropped and did not reappear until 1941.

## Inauguration of other Benefits under Part III of the Social Security Act.

### *Free Mental Hospital Treatment.*

On April 1, 1939, the first benefit was begun. Free treatment for all patients in the mental hospitals (a Government service and system) was made general.

### *Maternity Benefits.*

In April also it was announced that a beginning would be made with the maternity benefits, and an offer of contract was communicated to all practitioners by the Minister. Only 22 in the whole of New Zealand accepted the contract, the terms of which were generally held by the doctors to be very irksome to both practitioner and patient. It was also objected that there was no provision for consultant help, and some thought the fee of £5 per confinement with attendance before and after was inadequate.

After some weeks alternative proposals were brought forward to which the British Medical Association finally agreed. The general plan was payment per service rendered, and negotiations between the British Medical Association and the Government, lasting several months, were carried out in a spirit of reasonableness and moderation. The plan was made effective in November, 1939.

The scheme as thus amended dispenses with the necessity for the practitioner entering into a contract with the Government to render the services. All he has to do is to fill in a form with respect to each case of miscarriage or childbirth he attends, forward same to the local medical officer of health, and receive payments out of the social security fund. Complications and accidents are the subject of extra fees, as also the necessity for the help of an anæsthetist or consultant, and mileage. Obstetrical specialists under the scheme must be recognized as such by the Minister, according to standards of academic qualification and mode of practice laid down by the Health Department. Such a specialist attending a patient in childbirth is entitled to charge the patient fees in excess of those provided under social security, but no other doctor rendering "usual" maternity services may do so.

The fees are as follows:

1. "Usual" medical services: maternity, £5 5s.; miscarriage, £3.

2. In addition to these fees for "usual" services, toxæmia other than eclampsia, 10s. per visit with a maximum of £5; eclampsia £5; ante-partum hæmorrhage involving surgical intervention or blood transfusion, £4, with refund for donor and grouping tests; surgical induction of labour, £2; consultation, £1 1s.; anæsthetist, £1 1s.

3. Mileage. (The "chargeable distance" means the travelling distance, counted one way, exclusive of the first two miles, between the place where the patient is visited and the place of residence or surgery of the nearest practitioner in the scheme.) Where chargeable distance does not exceed two miles, £1 1s. to cover all visits; where more than two miles, 10s. 6d. for each mile or part of mile to cover all visits, and in other cases 4s. per mile of chargeable distance per visit.

All practitioners are considered to be serving under the scheme unless they "contract out" by giving notice of such intention. This process is not necessary for those, such as surgeons, who do not ordinarily practise midwifery. Similarly all patients are considered to be subjects of the scheme (if ordinarily resident in New Zealand) unless they signify their intention of paying their own fees.

The maternity scheme is fairly generally approved by both public and doctors. The rates of remuneration are considered by the doctors "satisfactory to good", for although the fees are not high, the certainty of being paid for every confinement attended is allowed to be the greater gain.

There is some lay criticism of the scheme on the financial aspects. It is said that in spite of the grant of money towards maternity home expenses, the patient is no better off, for the homes have raised their fees considerably. It is undoubtedly true that many small one-bed and two-bed maternity homes have been fortified or even created by the scheme. Licences, of course, are under the control of the Health Department.

Only a few are disturbed by the complacency of all concerned as to the efficacy of present modes of practice of obstetrics. It is important to provide for routine attendance for all, but it is also important to foresee trends in the development of the subject and make some attempt to follow them. The newer knowledge in obstetrics and gynæcology, particularly in respect of the hormones, is clearly grasped by very few practitioners, and even the "specialists" in obstetrics and gynæcology contrive, with few exceptions, to get on pretty well without it. No critical work is being done in this field on either clinical or laboratory aspects. One wonders whether it would not have been better, in the public interest, to have spent at least part of the social security money to help the growing points of the obstetric art and science. To have established in each or even in one of the remaining three large hospitals in New Zealand (Dunedin being the seat of the medical school), a unit devoted to clinical research into such subjects as the investigation of sterility, hormone treatment in obstetrics, and anæsthesia in childbirth, might in the long run do more good, both to the individual and to the community, than the present bread and butter measures. Such a unit, through post-graduate teaching and judicious publicity, might do an immense good in forestalling disasters and disappointments, and incidentally save its cost many times over through more accurate treatment, at present often blindly applied.

### *The Hospital Benefit.*

The hospital benefit was introduced in July, 1939. It made the services of the public hospitals free to all members of the community. No one is asked to pay for accommodation, maintenance or medical services. The anomaly by which out-patients but not in-patients were asked to pay for X-ray diagnosis and treatment was removed in 1941 by making these services also free to out-patients.

The change was made by the payment to the hospital boards—statutory local bodies—from the social security fund of 6s. per day per occupied bed and the abolition of patients' fees formerly charged.

This involves large sums of money—for example, the Auckland Hospital receives over £100,000 *per annum* from the social security fund. It is the first major change in hospital finance for many years. Formerly the boards found about half the money by local rates and received the rest from the consolidated fund, patients' fees being a small item and voluntary contributions almost negligible. There has been a slight reduction in local rates in some instances, but the mounting costs and more general use of the public hospitals render any real reduction unlikely.

So far there has been no greater control over the hospital system by the Government to go with this greater share in finance. The system as a whole, the constitution of the boards, the relation between boards and Health Department, and the standards in the individual hospitals have for many years stood in urgent need of overhaul and raising to modern standards.

Private hospitals have also shared in this benefit, for patients in them and in convalescent homes are eligible for the same 6s. per day. An eight-guinea room now costs the patient only six guineas, though hospital fees have been raised. The changes have led to the greater use of private hospitals—as of private maternity homes—and the position of the weaker ones has been confirmed.

In assessing the value to the people of these hospital benefits, it must be remembered that, particularly in some of the large cities, the public hospitals have lagged far behind modern standards and are feared by a proportion of the people. There is often no out-patient department at all, or, if present, it is often inadequately housed and staffed. In addition, the pressure on hospital beds, together with war conditions (military patients and absence of medical staff *et cetera*), makes the service often illusory. For months on end only patients with acute conditions will be admitted, and the patient with a hernia, for example, cannot claim his hospital benefit. In some instances there is a notorious absence of the best medical talent in the town from the hospital staff, and the public is well aware of this. In general, too, building programmes are years behind requirements and innumerable improvisations of accommodation commonly occur.

Another accompaniment of hospital benefits was the cessation of the honorary system of staffing. The part-time staff now receive varying sums (£500 to £600 *per annum* for a senior and £250 to £300 for an assistant physician or surgeon) for their work. In some instances, of course, there was already a full-time "closed staff". This carries on, and, as might be expected, it is usually overworked and sometimes underpaid.

*General Practitioner Service (First Version).*

With the outbreak of war and the dispatch overseas of a considerable number of medical men, nothing much was heard of further benefits for a period. At conferences with the Minister in February and August, 1940, the difficulties of the profession were described, but it became apparent that the Government was determined to proceed with a general practitioner service and that what might be acceptable to the profession was not acceptable to the Government.

In December, 1940, the *Finance Act* (Number 4), 1940, was passed making amendments to the *Social Security Act*, chiefly in relation to medical benefits or general practitioner service, but also mentioning free laboratory, X-ray and other services at the out-patient departments of public hospitals.

The general practitioner service was announced late in February, 1941, by the new Minister of Health, the Honourable A. H. Nordmeyer, to begin on March 1. It was to be a capitation system, available to all, remuneration to the doctor to be at the rate of 15s. *per annum* for every man, woman and child on his list, with extras for mileage. The contract was to be between patient and doctor, with free choice and right of refusal. The patient was to take a card to the doctor of his choice and have it countersigned. No limit was imposed on the doctor's list. There were a number of penalties for dereliction of duty.

British Medical Association spokesmen kept up hostile exchanges with the Government in the months preceding this announcement. The Government had not consulted the Association, the scheme was not a good one, and even if it were, it would be quite impossible for the doctors to undertake it, with 25% of their members and their most active section abroad on military service, and the remainder overworked with civil and military demands at home, to say nothing of immediate and remote demands which might be much heavier still.

The people were remarkably apathetic and were slow to enrol. The trades unions and others exerted pressure on their members to seek willing doctors. Wisecracks were uttered in the House by opposition Members of Parliament about "first catching your hare". As time went on it became apparent that only a few doctors were enrolling patients; in the largest city only one man; more in scattered country districts. In all, only forty to fifty men out of a possible seven hundred or eight hundred were found six months later to have undertaken the service.

In certain country districts, particularly one-doctor areas, the scheme is reported to be working well, having been embraced by all sections—political and social—of the community. The doctor is pleased with the more dignified relations with his patients and is often better off financially. No undue demands are made upon him. In the case of the urban men, good reports are also given, though in both cases it must be remembered that the men working the scheme were predisposed in favour of it.

Its failure as a general solution for the country led to the "second version", to be mentioned later. Opposition from the British Medical Association was determined, though no tremendous internal efforts were made to harden the front. Preoccupation and overwork on the part of the doctors kept many of them aloof from any active struggle.

There is no doubt that the people were surprised and disappointed that the onus had been placed on them to find their doctor, after paying the social security tax steadily for two years. Official British Medical Association comment at this stage ran as follows: "The Government was in the position of a broker who had sold to the public (and taken the money) something which he did not possess, had made no arrangements to obtain, and was unable to deliver. The position now is that the broker has confessed his inability to fulfil his contract, and says to his clientele: 'If you can get this for yourselves, I will pay.'"

The Government continued for some months to hope that the doctors would gradually come in, and as time went on began to issue threats of coercion, which rather inclined public sympathy towards the doctors.

*Pharmaceutical and Radiological Benefits.*

Regulations for pharmaceutical benefits were gazetted on April 22, 1941, and came into force on May 5, 1941. The chemists had little information before that date. Any chemist in business in the ordinary way may contract to provide the benefits, and all do. They are paid by the Government at their own rates less 2·5%, and seem very satisfied with the arrangements. They have a lot of clerical work, such as costing prescriptions item by item, and sending in copies to the Government, but business has considerably increased. The free use of "repeated" bottles has made the greatest difference to the total consumption. The opening of new pharmacies is under Government control, and there have been few new licences given.

Only drugs and preparations appearing in the British Pharmacopœia 1932 and *addenda* 1934 and 1940, and "Codex" 1934 are allowed on the free list. No proprietary product, except insulin, is allowed, nor serum, vaccine or antitoxin. Hormones, vitamin preparations and others, such as liver extracts, are excluded, as also the sulphonamides. Revision in respect of some of the last mentioned is promised, but six months after inauguration has not yet appeared.

There is no doubt that as a result of this benefit there has been a great increase in the demand for the "bottle of medicine" almost as a routine. Together with the non-availability of many of the genuine things of modern medicine, no great progress has resulted. No one seems to have thought of a national institute for the preparation, standardization and cheap distribution of, say, hormone preparations. Still less has anyone proposed a research institute in pharmacology as a national and perhaps international service in relation to this field.

In August, 1941, diagnostic services in the X-ray departments of the public hospitals were made free to all, as therapeutic services had already been made. This cleared up the anomaly that existed since hospital benefits were introduced, namely, that it cost a patient, say, two guineas as an out-patient of a public hospital to have his chest or stomach subjected to X-ray examination, whereas if he got himself admitted as an in-patient for a few days the whole cost him nothing.

The expected flood of work has not fully materialized, though it is quite clear that the volume will be considerably increased. Particularly in the larger hospitals, staff, room and plant are not nearly adequate for present needs, working under good conditions, let alone extra demands.

Radiologists in private practice are to be allowed to claim from the Government the same sums per service that are paid to the hospitals for X-ray work. These are detailed in a schedule, and are expected, under New Zealand conditions in private practice, to cover costs only. Radiologists will require to be recognized for the purpose by the Government and will be allowed to charge further fees to the patient over and above the sums mentioned. Final details of the Government allowances and extras chargeable remain to be fixed.

The arrangements were passed in Parliament before the radiologists commented on them. It is believed that a firm of dealers in radiological equipment and a hospital secretary advised the Government. The radiologists met soon after the enactment and are now conducting negctiations with the Government.

*General Practitioner Service (Second Version).*

A general election being due in November, 1941 (it was later postponed for twelve months), the tax for social security having been collected for more than two years and the promise of the main benefit (general practitioner service) being still unfulfilled, the Minister, the Honourable A. H. Nordmeyer, proposed at the end of August, 1941, a "fee-for-service" plan. The British Medical Association had not publicly altered its official plan of some four years' standing, but it was known that a section, chiefly general practitioners, was willing to consider a "fee-for-service" plan. There was a general dislike in the profession for a panel scheme of universal application, and the doctors still considered it a bad time to make any major change with 25% to 30% of doctors abroad or engaged full time in military duties at home.

The National Health Insurance Committee of the British Medical Association met the ministers towards the end of August and subsequently, but as the nature of the new proposals became apparent, hostility rapidly developed. The first version was that from a "bottomless pit" a fee of 5s. would be paid to the doctor per attendance at his rooms, 6s. 6d. in the case of a visit to the patient's house, and extras for mileage *et cetera*. It was to be illegal for a doctor to collect fees in any other way. A public outcry was raised, doctors, clergy, chambers of commerce *et cetera* joining in, and meetings were held all over the country. The Government gave in to the extent of raising the fee from 5s. to 7s. 6d., and 12s. 6d. for night and Sunday calls, and also in leaving it open for patients to enter into any private arrangements they liked with doctors. In this form the proposal became law in September as an amendment to the *Social Security Act*, the inauguration of the service being postponed from October 1 to November 1, 1941.

The British Medical Association announced publicly that practice would go on as usual from November 1. It has also sponsored a proposal that the whole matter be the subject of an investigation by a non-political commission.

At the time of writing (first week in November) many matters remain to be clarified. The British Medical Association realized that it must make an attempt to cooperate, though officially it disapproved of the scheme. Through its representations the conditions had been greatly ameliorated, and notable points had been scored over the Government. So much so that many of the laity think the rise from 5s. to 7s. 6d. to have been the only important matter—sufficient to turn a bad scheme into a good one in the eyes of the doctors. Though a doctor may, if he wishes, charge more than 7s. 6d., he has the legal right to sue for only 7s. 6d. This "denial of elementary British rights of access to the court for just reward of labour" has caused the British Medical Association to refrain meanwhile from sending representatives to the Government committee of control.

Two alternative ways of collecting the 7s. 6d. are allowed: (1) the patient signs a form to the effect that the doctor has rendered the service. The doctor lodges a pile of forms at, say, monthly intervals with the Social Security Department and is paid. (2) The doctor "carries on as usual", bills his patient 10s. 6d. or whatever he likes, and when paid gives a receipt to the patient. The patient then collects from the Post Office 7s. 6d. rebate per service.

The British Medical Association council has advised all divisions to ensure that their members adopt method (2). The argument is that practice is as before, and that if and when times of penury come, and the fee is lowered from 7s. 6d. to 5s. or 2s. 6d., the patient only is the loser. There is also a feeling that by avoiding "direct dealings with the department" more independence is maintained by the doctors.

Against this there are many doctors who prefer method (1), and groups even who seem determined to use it. They say the people will refuse to pay the bill at all, and so the doctor will get nothing; also that the trouble and cost of working method (2) will be infinitely greater than (1).

The attitude of the Government is not yet clear, but there are hints that the 7s. 6d. will be expected to be a full settlement, and that steps will be taken to prevent doctors using the 7s. 6d. as a new base-line and charging on top of that.

Innumerable points remain to be cleared up—the total cost of the scheme and how much abuse there will be *et cetera*. The position of the specialist is not clear. Most of his work lies outside the scope of the benefit, but can he and should he deprive a patient of his 7s. 6d. refund on a minor service, such as a post-operative or cancer follow-up observation?

In many ways this second version is less progressive or even more retrogressive than the first, when viewed from the standpoint of modern conditions. No help is given towards the cooperation of doctors in groups for mutual relief and better service. No mention is made of post-graduate training as an aid to high standards of work. No one seems to regard the scheme as in any way a final solution to the country's need in medical practice.

# Correspondence.

## SCARLET FEVER AND MIDWIFERY.

SIR: I would like to draw attention to a condition which may be a danger to our young mothers.

In Melbourne cases of scarlet fever are being refused by the infectious hospital. This means that the general practitioner has to attend them. He also has to attend midwifery cases.

I personally feel very worried when I have to attend a scarlet fever case and then a few hours after a confinement (twice lately).

May I suggest that a clear opinion be arrived at by expert pathologists concerning the risk of the doctor carrying infection. If there is a risk of carrying infection I think the present conditions must be improved. This might be by (*a*) adding to the accommodation of infectious hospitals, or (*b*) appointing a doctor (not connected in any way with midwifery) to whom the task of looking after home cases of scarlet fever could be allotted on the application of the patient's own doctor.

Yours, etc.,

October 25, 1941. "GENERAL PRACTITIONER."

## A NATIONAL MEDICAL SERVICE.

SIR: Reading Dr. Maude's remarks, and those of others, followed by the voluminous report of the Federal Council of the British Medical Association, one cannot help being struck with the underlying principle, which is that there is dissatisfaction with the present lack of coordination of health services.

It appears that the method of giving medical services is not satisfactory because a large percentage of the public cannot afford to pay the full cost of services required. A paragraph in *The Sydney Morning Herald* of October 25, at page 12, whilst forecasting nationalization of health services, is a vastly different idea from the Federal Council of the British Medical Association.

It is vague and gives no possible clue to any definite scheme.

No scheme so far sets out a perfectly satisfactory substitute for private medical practice, and in my view there is no substitute for it.

My suggestion is that there should be a supplementary scheme added to private practice.

I quite agree with Dr. Colville's remarks on page 515 of THE MEDICAL JOURNAL OF AUSTRALIA, November 1: "Private practice was a well-developed enterprise . . . Private practice was valued by many persons . . ."

I cannot see any reason to try to abolish private practice, when all that is needed is some method of providing for those who are unable to pay for all the related services.

One cannot help feeling that a national subsidy provided by the Federal Government would go a long way to covering the cost of what is now considered lacking. The subsidy could be made available as an annual part-time salary to all private practitioners, in proportion to the service rendered. This could be worked out by actuarial calculations, and rendered quarterly or otherwise, somewhat on the same lines as repatriation payments are at present paid.

This would not disturb private practice, but would be a means of amplifying it to meet altering needs.

It cannot be denied that the present economic system is being severely tried by war-time conditions; but that is no excuse for scrapping entirely a system which even under present admittedly remarkable strains, is standing up to the situation, and with modifications can be expected to see us through at least the war period.

Yours, etc.,

H. T. ILLINGWORTH.

Bruce Rock,
Western Australia,
November 6, 1941.

# Naval, Military and Air Force.

## APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 221, of November 6, 1941.

### ROYAL AUSTRALIAN AIR FORCE.

*Citizen Air Force: Medical Branch.*

Keith Gemmell Colquhoun, M.B., Ch.B., M.D., F.R.A.C.P., is appointed to a commission on probation with the rank of Flight Lieutenant, with effect from 13th September, 1941, and is promoted to the rank of Temporary Squadron Leader, with effect from 14th September, 1941.

The following are appointed to commissions on probation with the rank of Flight Lieutenant, with effect from the dates indicated: Dudley Owen Longmuir, M.B., B.S., 29th September, 1941; William Thomas Hudson Scales, M.B., B.S., 30th September, 1941.

The following are transferred from the Reserve to the Active List, with effect from the dates indicated: Flight Lieutenants A. E. Dickmann and D. McK. McNab, 29th September, 1941; T. W. Capell, 3rd November, 1941.

*Reserve: Medical Branch.*

The following is appointed to a commission on probation with the rank of Flight Lieutenant, with effect from the date indicated: Francis Winston Kiel, M.B., B.S., 25th September, 1941.

Pilot Officer J. W. L. Atkinson, M.B., B.S., is transferred from the Reserve, General Duties Branch, to the Reserve, Medical Branch, and is promoted to Flight Lieutenant, with effect from 25th September, 1941.—(Ex. Min. No. 157—Approved 5th November, 1941.)

### CASUALTIES.

ACCORDING to the casualty list received on November 17, 1941, Captain A. J. King, A.A.M.C., of Victoria Park, Western Australia, previously reported missing believed prisoner of war, is now reported prisoner of war.

## Notice.

### CLINICO-PATHOLOGICAL CONFERENCE.

THE next clinico-pathological conference arranged by the Post-Graduate Directors of Medicine, Surgery and Pathology will be held in the lecture hall at the Prince Henry Hospital, Little Bay, New South Wales, on Monday, November 24, 1941, at 4.30 p.m. The subjects will be cases for diagnosis and discussion. A cordial invitation to be present at the meeting is extended to all medical practitioners.

## Obituary.

### ARTHUR PAUL GILLESPIE.

WE regret to announce the death of Dr. Arthur Paul Gillespie, which occurred on November 12, 1941, at Goulburn, New South Wales.

### WILLIAM CHISHOLM.

WE regret to announce the death of Dr. William Chisholm, which occurred on November 13, 1941, at Sydney, New South Wales.

### CHARLES ELLIS JELBART.

WE regret to announce the death of Dr. Charles Ellis Jelbart, which occurred on November 10, 1941, at Albury, New South Wales.

## Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Hoy, Ronald James, M.B., B.S., 1939 (Univ. Sydney), General Post Office, Sydney.

The undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

Bligh, Richard Geoffrey, M.B., 1941 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Hellestrand, Alan Lacey, M.B., B.S., 1941 (Univ. Sydney), St. George District Hospital, Kogarah.

Vincent, George Kenneth, M.B., B.S., 1941 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Bryson, Allan Muir, M.B., 1939 (Univ. Sydney), 33, Elizabeth Street, Ashfield.

Rhydderch, Alun Iorwerth, M.B., B.S., 1941 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

## Books Received.

"The British Encyclopædia of Medical Practice, including Medicine, Surgery, Obstetrics, Gynæcology and other Special Subjects, Surveys and Abstracts, 1940, under the general editorship of Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., D.Sc., D.C.L., LL.D.; Publishing Editor: A. Clark, L.M.S.S.A.; Sub-Editor: G. Faulkner, D.Sc.; 1941. London: Butterworth and Company (Publishers) Limited. Super royal 8vo, pp. 659, with illustrations. Price: 33s. 6d. net.

"Medical Diseases of War", by Sir Arthur Hurst, M.A., D.M., F.R.C.P., with the co-operation of H. W. Barber, M.A., M.D., F.R.C.P., H. B. F. Dixon, M.C., M.D., D.T.M. and H., F.R.C.P., F. A. Knott, M.D., M.R.C.P., T. A. Ross, M.D., F.R.C.P., and A. W. Stott, M.A., F.R.C.P.; Second Edition; 1941. London: Edward Arnold and Company. Demy 8vo, pp. 435, with illustrations and diagrams. Price: 18s. net.

"Monographs from the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne; Number One: The Production of Antibodies: A Review and a Theoretical Discussion", by F. M. Burnet, M.D., Ph.D., with the collaboration of M. Freeman, B.Sc., A. V. Jackson, M.B., B.S., D. Lush, M.Sc.; 1941. Melbourne: Macmillan and Company Limited. Crown 4to, pp. 82, with diagrams.

"Sulfanilamide and Related Compounds in General Practice", by W. W. Spink, M.D.; 1941. Chicago: The Year Book Publishers Incorporated. Demy 8vo, pp. 256, with diagrams. Price: $3.0 net.

"The 1941 Year Book of Public Health", by J. C. Geiger, M.D., Dr.P.H.; 1941. Chicago: The Year Book Publishers Incorporated. Crown 8vo, pp. 544, with illustrations and diagrams.

## Diary for the Month.

Nov. 26.—Victorian Branch, B.M.A.: Council.
Nov. 27.—New South Wales Branch, B.M.A.: Branch.
Nov. 27.—South Australian Branch, B.M.A.: Branch.
Nov. 28.—Queensland Branch, B.M.A.: Council.
Nov. 28.—Tasmanian Branch, B.M.A.: Council.
Dec. 3.—Western Australian Branch, B.M.A.: Council.
Dec. 3.—Victorian Branch, B.M.A.: Annual Meeting.
Dec. 3.—Victorian Branch, B.M.A.: Council.
Dec. 4.—South Australian Branch, B.M.A.: Council.
Dec. 9.—Tasmanian Branch, B.M.A.: Branch.
Dec. 11.—New South Wales Branch, B.M.A.: Branch.
Dec. 12.—Queensland Branch, B.M.A.: Annual Meeting.

## Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

*New South Wales Branch* (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

*Victorian Branch* (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

*Queensland Branch* (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

*South Australian Branch* (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

*Western Australian Branch* (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

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